AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY

Editors

HOWARD C. TAYLOR, JR.

WILLIAM J. DIECKMANN

OFFICIAL ORGAN THE AMERICAN GYNECOLOGICAL SOCIETY

THE AMERICAN ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS NEW YORK OBSTETRICAL SOCIETY; OBSTETRICAL SOCIETY OF PHILADELPHIA BROOKLYN GYNECOLOGICAL SOCIETY; ST. LOUIS GYNECOLOGICAL SOCIETY NEW ORLEANS GYNECOLOGICAL AND OBSTETRICAL SOCIETY THE OBSTETRICAL AND GYNECOLOGICAL SOCIETY OF MARYLAND CHICAGO GYNECOLOGICAL SOCIETY: CINCINNATI OBSTETRIC SOCIETY CENTRAL ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY WASHINGTON GYNECOLOGICAL SOCIETY PITTSBURGH OBSTETRICAL AND GYNECOLOGICAL SOCIETY OBSTETRICAL SOCIETY OF BOSTON LOUISVILLE OBSTETRICAL AND GYNECOLOGICAL SOCIETY SOUTH ATLANTIC ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS SEATTLE GYNECOLOGICAL SOCIETY SOCIETY OF OBSTETRICIANS AND GYNECOLOGISTS OF CANADA ALABAMA ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS AKRON OBSTETRICAL AND GYNECOLOGICAL SOCIETY KANSAS CITY GYNECOLOGICAL SOCIETY CENTRAL NEW YORK ASSOCIATION OF GYNECOLOGISTS AND OBSTETRICIANS NEW JERSEY OBSTETRICAL AND GYNECOLOGICAL SOCIETY IOWA OBSTETRIC AND GYNECOLOGIC SOCIETY THE TEXAS ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS OKLAHOMA CITY OBSTETRICAL AND GYNECOLOGICAL SOCIETY MEMPHIS OBSTETRICAL AND GYNECOLOGICAL SOCIETY UTAH OBSTETRICAL AND GYNECOLOGICAL SOCIETY ROCHESTER OBSTETRICAL AND GYNECOLOGICAL SOCIETY ARKANSAS OBSTETRICAL AND GYNECOLOGICAL SOCIETY

Fox Chase
Philadelphia 11, Pa.

1

Published by The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, U. S. A.

TABLE OF CONTENTS ON PAGE 6

Copyright © 1956 by The C. V. Mosby Company



only pain is eliminated ...

with HEAVY SOLUTION

Nupercaine

When you provide saddle block anesthesia in obstetrical delivery, you assure "definite relief of pain . . . analgesia over the legs and thighs without causing paralysis of the muscles of the legs and thighs."

Supplied: 1:400 Nupercaine hydrochloride in 5% dextrose, 2-ml. ampuls, each ml. containing 2.5 mg. Nupercaine and 50 mg. dextrose; cartons of 10.

1. Causey, P. S., Reed, W. A., and Ford, J. L.: Arizona Med. 8:27 (Dec.) 1951.

C I B A SUMMIT, N. J.

2/2199M

Heavy Solution Nupercaine ® hydrochloride (dibucaine hydrochloride with dextrose 5% CIBA).

Vol. 72, No. 1, July, 1956. American Journal of Obstetrics and Gynecology is published monthly by The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Mo. Subscription rates: United States and its Possessions \$15.00, Students \$7.50; Canada, Latin-America, and Spain \$16.00, Students \$8.50; Other Countries \$17.50, Students \$10.00. Single copies \$2.50 postpaid. Entered as Second-Class Matter at Post Office at St. Louis, Mo., under Act of March 3, 1879. Printed in the U. S. A.







...and on the go

Modern, active, on the go... and pregnant. That's why she needs a vitamin-mineral supplement generously formulated especially for the stress of pregnancy.

Natalins-PF and Natalins are designed for the busy, modern woman. Small in size, they're easy to take. Just 1 capsule t.i.d. provides more than ample nutritional support.

specify

Natalins-PF

Mead phosphorus-free prenatal vitamin-mineral capsules

Contain calcium...
no phosphorus

or

Natalins®

Mead prenatal vitamin-mineral capsules

Contain both calcium and phosphorus



SYMBOL OF SERVICE IN MEDICINE

MEAD JOHNSON & COMPANY, EVANSVILLE 21, INDIANA, U.S.A.



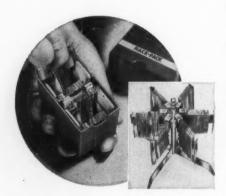
TO GET TO SURGERY

BARD-PARKER RIB-BACK

The state of the s

DETACHABLE SURGICAL BLADES

must 'survive' a rigid series of progressive scientific tests to qualify as suitable for surgical use. Those that 'pass' are surgically perfect and uniformly sharp throughout their entire cutting edge. They will remain sharp and useful for longer periods . . . an important factor in economy when yearly volume of purchases is considered.

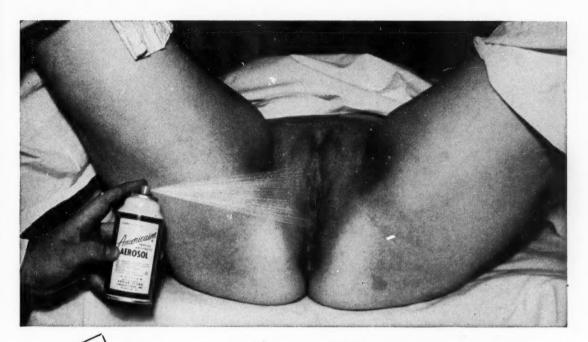


Specify RACK-PACK® packages in ordering gross and half gross quantities . . . eliminating unwrapping—handling—racking of individual blades. A time and labor saver for the O.R. personnel.

1ts Sharp

Ask your dealer

BARD-PARKER COMPANY, INC. Danbury Connecticut, U.S.A.



HOW TO COMFORT THE OB PATIENT AND SAVE NURSING TIME

In the past two years, hundreds of hospitals have adopted Americaine Aerosol as the routine spray-on relief for painful post-episiotomies, tender hemorrhoids, and fissured nipples.

Americaine Aerosol is the first aerosol preparation to be provided for this use. It offers the same potent topical agent as Americaine Ointment (20% dissolved benzocaine), and it is quick, easy to apply, and sanitary.

HOW TO GET BEST RESULTS AND ECONOMY IN APPLICATION

Americaine Aerosol is so easy to use, it can be applied by the nurse or by the patient, herself: Hold dispenser 8" to 12" from area and press button to release spray. Spray

sufficient to give good coverage without waste. Do not apply pad or other dressing for about 5 to 10 minutes after application, as this may soak up some of the medication and reduce effect. Do not hold dispenser upside down.

AMERICAINE AEROSOL FEATURES THAT MERIT YOUR ATTENTION

- Americaine provides relief in 2-3 minutes. Relief usually lasts 4-6 hours.
- 2. Americaine Aerosol should not be confused with any other aerosols or topical analgesics containing a much lower percentage of active drug. Only Americaine contains 20% dissolved benzocaine for faster, more prolonged relief
- Americaine is a simple, uncomplicated formula. This minimizes possibility of sensitivity. Not a single case of sensitivity was reported in 1866 published clinical cases. (Reprints on request.)

THERE IS A FREE AMERICAINE AEROSOL FOR YOU Please enclose prescription blank when requesting



SMALL SIZE!

New 3 oz. dispenser is easy for patient to use.

Americaine AEROSOL

NOW. THREE SIZES: 11 oz. size for professional use and floor stock, 5.5 oz. and 3 oz. sizes for your prescriptions,

ARNAR-STONE LABORATORIES, INC., Mount Prospect, Illinois

The New Clinically Proved

"MOGEN" CIRCUMCISION INSTRUMENT

designed by HARRY BRONSTEIN*

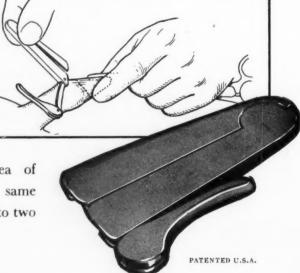
Circumcision, at one time a religious ritual among a few faiths, today is a routine universal practice. The procedure, though a simple operation, has been impeded by the lack of a safe and effective, yet simple instrument.

The "MOGEN" Circumcision Instrument reduces the technique circumcision to a simple procedure. With the use of the "MOGEN," the physician can now perform the entire operation safely—swiftly—simply. Clinical tests have proved that the entire procedure can be performed in approximately one minute—even without previous experience.

The "MOGEN" Circumcision Instrument, clinically tested on more than 700 babies, assures complete, quick hemostasis at the line of circumcision. Its practical design and sturdy construction prevent side-slipping; beveled underedge and precision-engineered aperture prevents accidental injury to glans

penis, while its flat surface assures accurate, clean, even excision of prepuce. The "MOGEN," constructed of stainless steel in a single unit, allows for precise gaging of prepuce and mucosa to be excised—

the physician sees entire area of operation at all times. This same unit is adaptable for babies up to two years of age.



For further information and literature write to:

HARRY BRONSTEIN 329A CROWN STREET, BROOKLYN 25, N. Y. SLocum 6-5969

^{*}Guest lecturer on circumcision in medical schools

setting new standards

ETHICON

sutures

ATRALOC needles

ETHICON

NOW Bactericidal! Fungicidal! DERMOPLAST**

TOPICAL ANESTHETIC

*without phenol anti-pruritic astringent

IN THE NEW 3 OZ. PRESCRIPTION SIZE

for individual therapy in hospital and home

PROVIDES NEW RELIEF
OF SURFACE PAIN AND ITCHING
WITHOUT TOUCHING AFFECTED AREAS

perineal suturing hemorrhoids pruritus ani pruritus vulvae wounds burns abrasions sunburn



Formula: benzocaine 4.7%; benzethonium chloride 0.1%; menthol 0.5%; ephedrine alk. 0.125%; dissolved in oils (Doho process).

Substantiating clinical data sent on request.

DOHO
100 VARICK ST.
NEW YORK 13, N. Y.

CONTENTS FOR JULY, 1956

Original Communications

The Use of Unlimited Nonsterile Vaginal Examinations in the Conduct of Labor. Frank J. Fara, M.D., Marsh Steward, Jr., M.D., and John Standard, M.D., Chicago, Ill.
Is the Standard of Obstetric Morbidity Serving a Useful Purpose? Irving Siegel,
M.D., Chicago, Ill. Cesarean Section in Multiple Pregnancies. Simon Brody, M.D., Brooklyn, N. Y. Rupture of the Gravid Uterus. Frederick J. Maisel, M.D., Baldwin, N. Y. Brow Presentation. Lawrence H. Madden, Jr., M.D., Pittsburgh, Pa. Shoulder Presentation. Augusta Webster, M.D., and W. F. Geittmann, M.D., Chi-
cago, Ill. The Metabolism of Urate in Pre-eclampsia. Joseph Seitchik, M.D., Philadelphia, Pa. Further Experience With Apresoline in Toxemia and Hypertension of Pregnancy. Humbert L. Riva, Lieutenant Colonel, MC, USA, Woodrow L. Pickhardt, Lieutenant Colonel, MC, USA, Robert H. Holzworth, Captain, MC, USA, and Robert L. Sherman, Major, MC, USA, Washington, D. C.
Retention Catheter Following Vaginal Delivery. J. Kenneth Patterson, M.D., Santa Barbara, Calif.
Barbara, Calif. Maternal Factors in Prematurity. Clair E. Folsome, M.D., Martin L. Stone, M.D., Leonard Hirsch, M.D., and Burton Krumholz, M.D., New York, N. Y.
Duration of Pregnancy for Cleft Palate Children. Kenneth R. Lutz, A.M., Onawa, Iowa, and C. E. Francis, M.D., Loma Linda, Calif.
Comments on the Richardson Pregnancy Test and the Rapp-Richardson Saliva Prenatal Sex Determination Test. W. G. Dobson, M.D., and A. G. Gornall, Ph.D.,
Toronto, OntarioExperimental Amniotic Fluid Infusion. Robert M. Hunter, M.D., John C. Scott,
Ph.D., John P. Schneider, V.M.D., and John A. Krieger, M.D., Philadelphia, Pa. Studies on Peritoneal Fluid in the Pregnant Rat. Jacques Padawer, Ph.D., and
Albert S. Gordon, Ph.D., New York, N. Y The Uterine Omentum of the Rat and Its Response to Vasoconstrictor Drugs.
Robert Landesman, M.D., and Barbara Mendelsohn, A.B., New York, N. Y Pregnancy Complicated by Amyotrophic Lateral Sclerosis. J. Wilson Huston, Commander (MC) USN, John Lingenfelder, M.D., Corpus Christi, Texas, and
Donald W. Mulder, M.D., and Leonard T. Kurland, M.D., Rochester, Minn. Treatment of Cancer of the Cervix Uteri. Professor M. A. van Bouwdijk Bastiaanse, Amsterdam, Holland Carcinoma of the Cervix With Early Stromal Invasion. Charles B. Wheeler, Jr.,
M.D., Kansas City, Mo.
Surgery as an Adjunct to Irradiation Therapy in Carcinoma of the Cervix. Edward J. Crawford, Jr., M.D., Lewis S. Robinson, M.D., and Lloyd A. Hornbuckle, M.D., Shreveport, La.
Primary Carcinoma of the Fallopian Tube. Arthur N. Frankel, M.D., New York, N. Y. Ovarian Tumors and Abnormal Uterine Bleeding. Melvyn A. Bayly, M.D., and R. R. Greene, M.D., Chicago, Ill.
External Endometriosis and Abnormal Uterine Bleeding. Melvyn A. Bayly, M.D., and Larry L. Gossack, M.D., Chicago, Ill.
Hodgkin's Disease as It Affects the Physiology and Anatomy of the Female Generative Tract. James P. Hennessy, M.D., and Antonio Rottino, M.D., New
York, N. Y. Pathogenesis of Polycystic Ovaries. Sheldon C. Sommers, M.D., and Percy J. Wadman, M.D., Boston, Mass.
The PSP (Phenolsulfonphthalein) Test for Tubal Patency. George Speck, M.D.,
and Paul E. Halter, M.D., Arlington, Va. Physiologic Endosalpingitis? H. A. Smith, M.D., and R. R. Greene, M.D., Chicago, Ill.
Department of Case Reports
New Instruments, Etc.
Chorionepithelioma Following Full-Term Pregnancy. A. E. Kanter, M.D., and Robert Bauer, M.D., Chicago, Ill. Normal Pregnancy After Recovery From Metastatic Choriocarcinoma. William B. Patterson, M.D., Puunene, Maui, Hawaii Status Epilepticus and Pregnancy. Milton D. Klein, M.D., Milton J. Goodfriend, M.D., and Irving A. Shey, M.D., New York, N. Y.
(Continued on base 8)



EASIER CONTROL OF SUMMER-TIME ALLERGIES

For the quick relief which ACTH gives in summer-time allergies, with minimal inconvenience to your patient, use Cortrophin-Zinc. Its prolonged action permits maximal response in rose fever, poison ivy, poison oak, sumac, asthma, and other allergic manifestations, with fewer injections. Each injection lasts at least 24 hours in the most acute cases to 48 and even 72 hours in milder cases. And Cortrophin-Zinc is easy to use, being an aqueous suspension which requires no preheating and flows easily through a 26-gauge needle.

CORTROPHIN*ZINC'



HAY FEVER

POISON IVY

POISON OAK OR SUMAC

SEASONAL ASTHMA

ROSE FEVER

Supplied in 5-cc vials, each cc containing 40 U.S.P. units of corticotropin adsorbed on zinc hydroxide (2.0 mg zinc/cc)

*T.M.-Cortrophin

†Patent Pending. Available in other countries as Cortrophine-Z.

†Organon brand of Corticotropin-Zinc Hydroxide

an Organon development

ORGANON INC. · ORANGE, N. J.

CONTENTS (Continued from page 6)

Report of a Case of Simultaneous Tubal and Intrauterine Pregnancies. J. Viviano, M.D., St. Louis, Mo.
Condyloma Acuminatum in Pregnancy Treated With 20 Per Cent Tincture Podophyllin. Anthony C. Milea, M.D., New York, N. Y.
A Pubotractor for Inspection of the Postpartum Cervix. R. C. Creelman, M. Bremerton, Wash.
Muscular Torticollis—Congenital Disease or Birth Injury? George L. Moore, M. Bellaire, Texas
Successful Postmortem Cesarean Section. John V. Kelly M.D., Grosse Pointe, Mic and Herbert G. Winston, M.D., Scarsdale, N. Y.
An Unusual Case of Exudative Vaginitis (Hydrorrhea Vaginalis) Treated W Local Hydrocortisone. Lewis C. Scheffey, M.D., A. E. Rakoff, M.D., and Warr R. Lang, M.D., Philadelphia, Pa.
Agenesis of Müllerian Ducts With Report of Case. Roy L. Grogan, M.D., F. Worth, Texas, and Truman C. Blocker, M.D., Galveston, Texas
Department of Reviews and Abstracts
Review of New Books
Selected Abstracts
Solvette assessment and a second and a second and a second assessment assessment assessment as a second as
Correspondence
Correspondence

American Journal of Obstetrics and Gynecology

Editors: HOWARD C. TAYLOR, JR., and WILLIAM J. DIECKMANN

ADVISORY COMMITTEE ON POLICY 1956

Willard M. Allen John I. Brewer Francis Bayard Carter Conrad G. Collins Nicholson J. Eastman Frank R. Lock Newell W. Philpott John Rock Donald G. Tollefson

ADVISORY EDITORIAL COMMITTEE 1956

Albert H. Aldridge
Edward Allen
Allan C. Barnes
Leroy A. Calkins
Russell R. de Alvarez
R. Gordon Douglas
George H. Gardner
Louis M. Hellman
Carl P. Huber
Frank R. Lock
Curtis J. Lund

Andrew A. Marchetti
Harvey B. Matthews
John L. McKelvey
Charles E. McLennan
Joe Vincent Meigs
William F. Mengert
Norman F. Miller
Thaddeus L. Montgomery
Daniel G. Morton
Emil Novak
Ernest W. Page

Franklin L. Payne
Lawrence M. Randall
Duncan E. Reid
Ralph A. Reis
Herbert E. Schmitz
George V. Smith
Wm. E. Studdiford
E. Stewart Taylor
Richard W. Te Linde
Herbert F. Traut



for the modern woman...a modern prenatal supplement

Today's pregnant woman is more fortunate than her sister of yesteryear . . . she looks better, feels better and enjoys greater freedom during her pregnancy. She is free, too, from such traditional prenatal distress as leg cramps, irritability and mild edema when a *modern* prenatal supplement is prescribed.

Usable calcium—Recent evidence points to a new rationale of prenatal nutrition. "... it is apparent that dicalcium phosphate, so widely used as a dietary supplement in pregnancy, is undesirable."* Calcisalin, for routine prenatal supplementation, provides calcium in the usable form of the lactate salt, rather than phosphate.

The complete prenatal supplement — Calcisalin also provides reactive aluminum hydroxide gel (to absorb excess dietary phosphorus) and the minimum daily vitamin and iron allowances for pregnancy as recommended by the National Research Council.

Thus the risk of inadvertently raising the phosphorus level to the point where it interferes with calcium absorption is avoided with Calcisalin.

Dosage: Two tablets three times daily after meals. Available: Bottles of 100 tablets and 8-oz. reusable nursing bottles containing 300 tablets.

*Page, E. W., and Page, E. P.: Obstet. & Gynec. 1:94 (Jan.) 1953.

Calcisalin®

WARNER-CHILCOTT

A brighter outlook comes with a "sense of well-being"



Every woman who suffers in the menopause deserves "Premarin."

"Premarin" provides prompt relief from distressing symptoms and an added "sense of well-being."

"Premarin," available as tablets and liquid, presents the complete equine estrogen-complex. Has no odor, imparts no odor.



in the menopause and the pre-and postmenopausal syndrome



AYERST LABORATORIES . New York, N. Y. . Montreal, Canada

5643

In deference to her daintiness . . .

- Massengill Powder is buffered to *maintain** an acid condition in the vaginal mucosa.
- Massengill Powder has a low surface tension which enables it to penetrate into and cleanse the folds of the vaginal mucosa.
- Massengill Powder has a "clean" antiseptic fragrance. It enjoys unusual patient acceptance.
- Massengill Powder solutions are easy to prepare. They are nonstaining, mildly astringent.

massengill powder®

when recommending a vaginal douche

indications:

Massengill Powder solutions are a valuable adjunct in the management of monilia, trichomonas, staphylococcus, and streptococcus infections of the vaginal tract. Routine douching with Massengill Powder solutions minimizes subjective discomfort and maintains a state of cleanliness and normal acidity without interfering with specific treatment.

*In a recent clinical report, ambulatory patients—with an alkaline vaginal mucosa resulting from pathogens—maintained an acid vaginal mucosa of pH 3.5 for 4 to 6 hours after douching with Massengill Powder; recumbent patients maintained a satisfactory acid condition up to 24 hours.

Generous samples on request.

The S.E. MASSENGILL Company

Bristol, Tennessee

New York

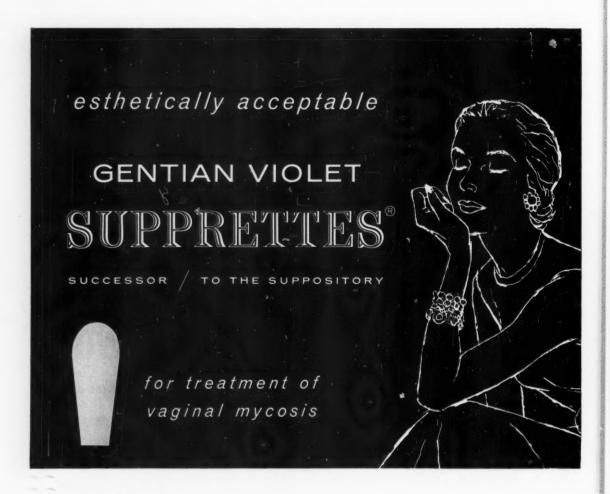
Kansas City

San Francisco

July, 1956

nec.

Page 11



Gentian Violet Supprettes are preferred by physicians for maximum fungicidal activity . . . by patients for minimal messiness

Gentian Violet Supprettes provide rapid relief from itching, burning, and discharge without irritation to vaginal membranes. Effective even in resistant cases of monilial vaginitis. Messiness and cost are less than with other gentian violet preparations.

Composition: Each Supprette contains gentian violet 0.2%, lactic acid 0.3%, and acetic acid 1.0%. Supplied: In jars of 12.

- Pregnancy moniliasis
- Antibiotic moniliasis
- Mycotic leukorrhea
- Diabetic vulvitis
- Mycotic vulvovaginitis
- Pruritus vulvae

The "Neocera" Base **Makes the Difference**

Contains no oils or fatty materials. Consists of water-soluble Carbowaxes* with active dispersal agent. Mixes completely with vaginal and cervical fluids to assure thorough penetration into folds of vaginal

*Trademark U.C.C.

GENTIAN VIOLET SUPPRETTES

NO REFRIGERATION NECESSARY . Samples on Request

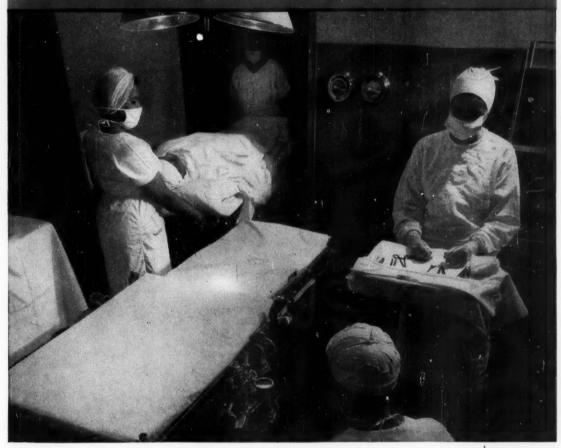


THE WILLIAM A. WEBSTER COMPANY . MEMPHIS 5, TENNESSEE

Mephyton (VITAMIN KJ. MERCK)

Preferred product for routinely stabilizing prothrombin levels before surgery

MAJOR ADVANTAGES: Action detectable within 15 minutes; complete reversal of hypoprothrombinemia within 4-12 hours.



There are three significant reasons for preferring Mephyton over the menadione derivatives. The action of Mephyton is: (1) more rapid, (2) more complete, and (3) more prolonged. These advantages apply to either simple vitamin K deficiency states or in anticoagulant-induced hypoprothrombinemia. In the latter condition, Mephyton provides the *most* dependable and practical means of restoring normal levels of prothrombin.

INDICATIONS: Hypoprothrombinemia due to Dicumarol®, Cumopyran®, Hedulin®, Tromexan®, antibiotics, salicylates, obstructive

jaundice, hepatic disease, impaired gastrointestinal absorption, and deficiency of vitamin K in the newborn.

SUPPLIED: In boxes of six 1-cc. ampuls, each cc. containing 50 mg. of vitamin K_1 .



PHILADELPHIA 1, PA.
DIVISION OF MERCK & CO., INC.

July, 1956

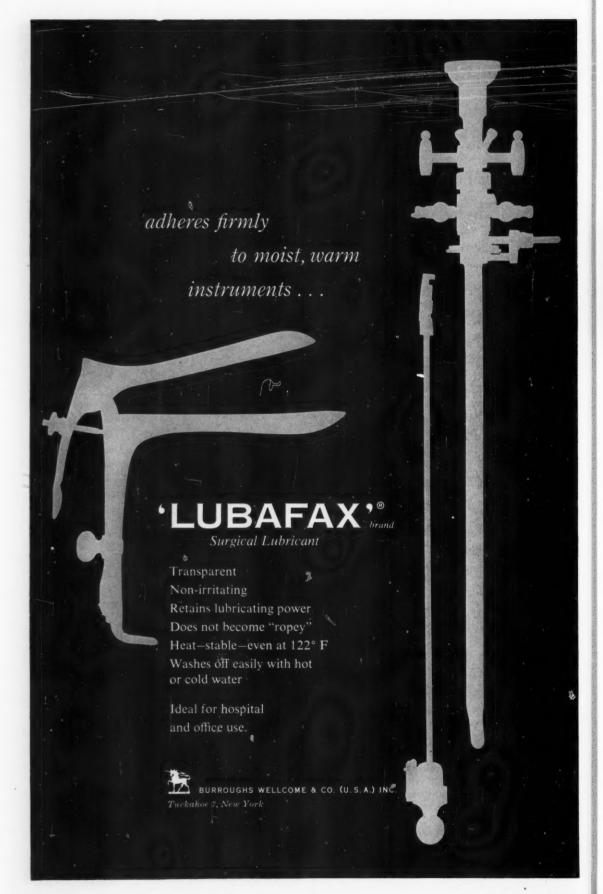
ely

nal

SEE

ec.

Page 13



"... may be unique as a wide-spectrum antimicrobial agent that is bactericidal, relatively nontoxic, and does not invoke resistant mutants."

Furadantin

in acute and chronic pyelonephritis, cystitis, prostatitis

Percentage of Effectiveness of Furadantin Against Various Strains of Bacteria in Vitro

	Aerobacter aerogenes	Proteus sp.	Paracolo- bactrom sp.	Micro- coccus pyogenes	Strepto- coccus pyogenes	Esche- richia coli	Pseudo- monas aeruginoss
Furadantin	82.1	66.6	31.2	91.9	93.9	60.0	13.3
Antibiotic A	71.4	55.5	25.0	93.5	96.9	66.0	26.6
Dihydrostreptomycin	14.2	25.9	12.5	38.7	27.2	28.0	6.6
Antibiotic B	3.5	0	0	66.1	63.6	0	2.2
Penicillin	3.5	0	0	27.4	39.3	0	0
Antibiotic C	14.2	7.4	18.7	46.7	72.6	22.0	11.1

ADAPTED FROM PERRY2

Furadantin's "high degree of effectiveness against bacteria responsible for urinary tract infections is brought out by this study." 2

Furadantin dosage—simple and safe: Average adult dose is 100 mg., q.i.d., (at mealtime, and on retiring, with food or milk). Average daily dosage for children is 5 to 7 mg./Kg. in four divided doses.

SUPPLIED: Tablets, 50 and 100 mg., bottles of 25 and 100. Oral Suspension, 5 mg. per cc., bottle of 118 cc.

REFERENCES: 1. Waisbren, B. A., and Crowley, W.: A.M.A. Arch. Int. M. 95:653, 1955. 2. Perry, R. E., Jr.: North Carolina M. J. 16:567, 1955.

NITROFURANS-A NEW CLASS OF ANTIMICROBIALS-NEITHER ANTIBIOTICS NOR SULFAS

Eaton

July, 1956

ynec.

Page 15



CREAM • STERILE JELLY • COMPOUND LOTION (calamine, zinc oxide, menthol added)

SUBJECT: How Tronothane makes surface anesthesia more useful to the physician

Dear Doctor:

There are many potent surface anesthetics on the market. Why, then, has Abbott introduced Tronothane in such a crowded field?

The answer is that Tronothane was created to fill a conspicuous gap among surface anesthetics. It is designed to combine

- (a) good relief from pain or itching, with
- (b) relative freedom from the toxic or allergic reactions that may accompany some of these other agents.

This was done by synthesizing Tronothane as a totally new and unique compound, far removed from the "caine" type drug.

Tronothane has been proved to give ample relief of discomfort in many common conditions: itching dermatoses, anogenital pruritis, painful episiotomy, hemorrhoids, rectal surgery, etc.

In the clinical reports, covering over 15,600 cases, toxicity was not observed and sensitization was negligible. Patients already allergic to other local anesthetics used Tronothane with excellent results.

But look into this helpful agent for your own practice soon.

Yours truly,

ABBOTT LABORATORIES

P.S. This is the sunburn, poison ivy season, Tronothane's soothing compound lotion is particularly useful. Flesh-toned, never greasy, it resists rubbing off on clothes.

NEW

Against Disease and Discomfort
in urinary tract infections

Azo Gantrisin, in one tablet, combines
Gantrisin with a widely-used urinary tract
analgesic. The high plasma and
urine levels achieved by Gantrisin
effectively combat urinary infections
both systemically and locally.
The rapid local action of the analgesic
dye is reflected by the early appearance of
an orange-red color in the urine.
Each Azo Gantrisin tablet contains 0.5
Gm Gantrisin 'Roche' plus 50 mg phenylazodiamino-pyridine HCl.

'Roche' Original Research in Medicine and Chemistry

For patients harrisd by hurry and worry —

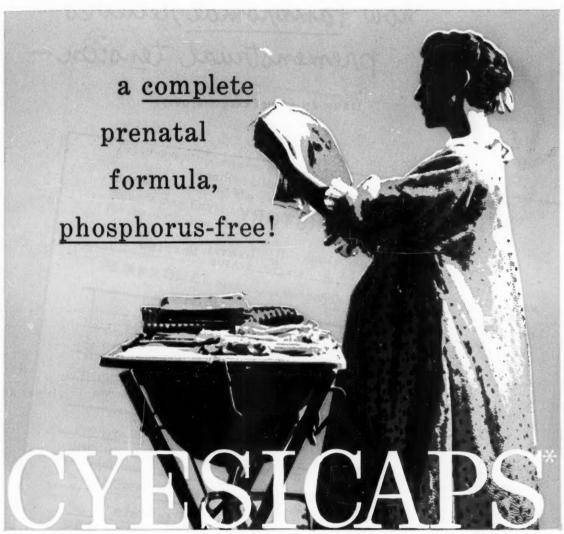
Noludar 'Roche' brings calm and quiet. Not a barbiturate, not habit forming, 50 mg t.i.d. provides daytime sedation with little or no loss of acuity, or 200 mg h.s. induces a sound night's sleep with a refreshed and clear-headed awakening.

Noludar tablets, 50 and 200 mg; elixir, 50 mg per teaspoonful.

elixir, 50 mg per teaspoonful.
Hoffmann-La Roche Inc, Nutley,

Noludar brand of methyprylon





PRENATAL VITAMIN-MINERAL CAPSULES LEDERLE

Civ aspeules supplu

If you find your patients complain excessively of muscle cramps due to high phosphorus intake, prescribe CYESICAPS. Each capsule provides 22 vitamins and minerals plus purified intrinsic factor concentrate; calcium is supplied as calcium lactate, its most readily assimilated form. This well-balanced formula is indicated throughout pregnancy and lactation.

Dosage: 1 or 2 capsules 3 times daily.



dry- filled sealed capsules

a Lederle exclusive, for more rapid and complete absorption. No oils, no paste, no aftertaste!

Six capsules supply:
Calcium (as Lactate) 600 mg.
Calcium Lactate 3720 mg.
Intrinsic Factor Concentrate 1.5 mg.
Vitamin A 6,000 U.S.P. Units
Vitamin D 400 U.S.P. Units
Thiamine Mononitrate (B ₁) 1.5 mg.
Riboflavin (B ₂) 3 mg.
Niacinamide 15 mg.
Vitamin B ₁₂ 6 mcgm.
Ascorbic Acid
Folic Acid
Pyridoxine HCl (B ₆) 6 mg.
Calcium Pantothenate 6 mg.
Vitamin K (Menadione) 1.5 mg.
Iron (as FeSO ₄ exsiccated)
Vitamin E (as Tocopheryl Acetate) 6 I.U.
lodine (as KI) 0.1 mg.
Fluorine (as CaF ₂) 0.09 mg.
Copper (as CuO) 0.9 mg.
Potassium (as K ₂ SO ₄) 5 mg.
Manganese (as MnO ₂) 0.3 mg.
Magnesium (as MgO) 0.9 mg.
Molybdenum (as Na ₂ MoO ₄ .2H ₂ O) 0.15 mg.
Zinc (as ZnO)
•Reg. U.S. Pat. Off.
Reg. U.S. Pat. On.



LEDERLE LABORATORIES DIVISION AMERICAN Cyanamid company PEARL RIVER, NEW YORK

July, 1956

Page 17

how Pambromal relieves premenstrual tension -



(FROM AN ACTUAL CASE HISTORY)

CASE HISTORY

	MARITAL Married
	AGE 31 y. sex F. status Married
ME_L.W.	AGE
1/25/55	
TE	emotional basis.
	Alimentary obesity on emotional basis.
IAGNOSIS	Allmos Pre-
	denate dysmenorrhea.
	Obesity. Moderate dysmenorrhea. Pre-
COMPLAINTS	Obesity. Moderate menstrual tension with bloating.
PHYSICAL EXAMINATION_	Negative.
	104
THERAPY	Placed on 1000 calorie dans tablets amine. Thyroid. Pambromal tablets
	amine. Thyrola.
	amine. Thyroid. Pambromar amine. Thyroid. Pambromar (2 to 3 tabs. a day) to be taken 1 week
	before menses.
	Striking relief 110m stated that it was
	Striking relief from all P Striking relief from all P symptoms. Patient stated that it was that she had had any relief
	from her premenstruct
	Lost 35 lbs. No complaints.
1	10/27/55. Lost 30 2

WHITTIER LABORATORIES . CHICAGO 11, ILLINOIS



COMMENT:

The premenstrual tension syndrome, in many instances, is an incidental complaint. The patient often consults the physician for some unrelated disease. In spite of the emotional problems it creates, quite a few patients may forget mentioning their distress unless specifically asked Now, relief can be given and it is deeply appreciated...

PAMBROMAL neutralizes the antidiuretic hormone

		uretic hormon	е
Diuresis without pamabrom	subject 1	subject 2	
,dbrom	106 cc.		subject 3
Diuresis with		275 cc.	210 cc.
pamabrom (100 mg.)	950		
	950 cc.	980 cc.	10.
pjects were given 1000 c			1200 cc.

Subjects were given 1000 cc. of water and injected with antidiuretic hormone (pitressin). When pamabrom (an ingredient of Pambromal) was administered, the water-retaining effect of the antidiuretic hormone was almost completely neutralized.

(Bickers, W., and Wood, M.: New England J. Med. 240: 453, 1951)

PAMBROMAL controls nervous system lability

Contains both dextro-amphetamine sulfate and carbromal, a reliable sedative...counteracts irritability, anxiety and fatigue...relaxes

PAMBROMAL relieves pain more effectively

Contains salicylamide—a time-tested and proven analgesic considerably more potent than other salicylates.

Each tablet contains: Pamabrom (to neutralize the ..50 mg. antidiuretic hormone) Dextro-amphetamine sulfate (to elevate mood)......2.5 mg. Carbromal (to relax tension)...130 mg.

Salicylamide (to relieve pain) . . 250 mg.

Bottles of 24 and 100

tie

PAMBROMAL® tablets (

R a U

A FIRST THOUGHT IN
HYPERTENSION
EVERY GRADE...
EVERY TYPE

original alseroxylon

all the desirable alkaloids of India-grown Rauwolfia serpentina, Benth.

mutually potentiated action

high clinical efficacy because of interpotentiation of contained alkaloids

freed from undesirable alkaloids

yohimbine-like and other undesirable substances in the Rauwolfia root are removed

virtually no serious side actions

when side actions are encountered, they are notably mild

especially suitable for long-term therapy

no alteration in patients' tolerance, no chronic allergic toxicity, no latent undesirable actions



LOS ANGELES

easy to prescribe

simple regimen—merely two 2 mg. tablets at bedtime; for maintenance 1 tablet usually suffices.

July

Makes her fancy for daintiness a fact in your prescription success.

new!

Your patients will appreciate the new LANTEEN Easy-clean applicator for one simple but important reason—unlike other applicators it can be disassembled and cleaned thoroughly. This considerate improvement lets your patient know that you appreciate her fancy for daintiness, while you insist on her observing strict feminine hygiene. Another LANTEEN design for better patient-cooperation.

Easy-clean jelly applicator.



LANTEEN jelly, diaphragms, and jelly-diaphragm sets are distributed by George A. Breon & Company, 1450 Broadway, New York 18, N. Y. (In Canada: E. & A. Martin Research Ltd., 20 Ripley Ave., Toronto, Canada) Manufactured by Esta Medical Laboratories, Inc., Chicago 38, Ill.

SS 1334 - 7336

nec.



Certainly there are few times when milk nourishment is as important as it is during pregnancy . . . and few times when nutritive values must be weighed so

carefully against caloric intake.

And the nourishment in *Instant* Pet Nonfat Dry Milk fits this time exactly.

For the expectant mother concerned with problems of overweight, *Instant* Pet makes nonfat milk with delicious fresh-milk flavor . . . with *all* milk's protein, calcium, B-vitamins . . . and with only *balf* the calories of whole milk,

Also, for the mother who doesn't drink enough milk, Instant Pet Nonfat Dry Milk supplies these important nutrients in highly concentrated form . . . ideal for fortifying milk-made dishes or beverages, and for inclusion in dishes not usually made with milk.

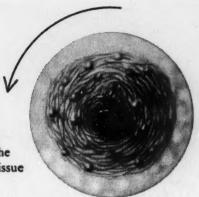
And whether used as a delicious beverage or as an ingredient in foods, *Instant* Pet supplies this nourishment at surprisingly low cost . . . as little, in fact, as 8 cents per reconstituted quart.

Instant PET NONFAT DRY MILK supplies essential milk nourishment with minimum caloric intake at minimum cost.



PET MILK COMPANY • ARCADE BUILDING • ST. LOUIS 1, MISSOURI

Jul

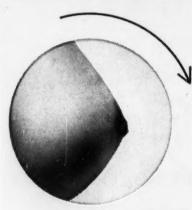


FISSURED NIPPLE THERAPY

The use of White's Vitamin A & D

Ointment soothes and softens the
fissured nipple, promotes tissue
regeneration.

WHITE'S VITAMIN A & D OINTMENT



t

lk

of

n,

lk,

t

RI

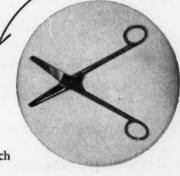
dynec

NIPPLE ROUTINE

—a valuable and simple prophylactic measure against drying, fissuring and erosion.

AFTER EPISIOTOMIES

As a post-surgical dressing,
White's Vitamin A & D Ointment
provides comfort for the patient and
encourages rapid healing.



Specify White's Vitamin A & D Ointment also in such conditions as burns, diaper rash, chafing, indolent ulcers.

Recommend the 1½ or 4 oz. tubes; the 1 lb. or 5 lb. jars.



WHITE LABORATORIES, INC./KENILWORTH, NEW JERSEY

July, 1956

Page 23

"the gratitude of the patient is ample reward"...

"Vaginal discharge is a common complaint amongst
women of all ages ... this is one of the conditions
in which the gratitude of the patient is ample
reward for the time and trouble spent in treatment,"
states one investigator. Gantrisin Vaginal
Cream is highly effective against
many sulfonamide-susceptible
microorganisms which are
frequently found in vaginal and
cervical infections. Its acid
pH of 4.6 promotes the return
of the flora found in a
healthy vagina.
Gantrisin -- brand of
sulfisoxazole

Hoffmann - La Roche Inc

Nutley . N.J.



THORAZINE*

controls nausea and vomiting in obstetrics

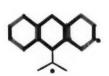
Reduces vomiting during all 3 stages of labor

'Thorazine' reduces both the incidence and severity of nausea and vomiting, lessening a potential anesthetic hazard without harmful effect on mother or child.¹

Speeds recovery after delivery

By controlling post-partum nausea and vomiting, 'Thorazine' speeds the patient's return to normal eating habits, resulting in a brighter outlook and often a shorter hospital stay.

'Thorazine' is available in ampuls, tablets and syrup, as the hydrochloride; and in suppositories, as the base.



1. Karp, M., et al.: Am. J. Obst. & Gynec. 69:780 (April) 1955

 $Smith, Kline\,\&\,French\,\,Laboratories,\,Philadelphia$

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

How CARNATION INSTANT provides new dietary advantages not possible with other forms of nonfat milk

Because Carnation Instant is a new crystal form of nonfat dry milk, the physician may specify a greater ratio of milk solids to water than

supplied by bottled nonfat milk. The new crystal form may also be added to *whole* milk to increase its nutritive content.





WHEN LIQUIDS ARE RESTRICTED,

the physician may specify an additional heaping tablespoon of Carnation crystals per glass (or $\frac{1}{3}$ cup additional crystals per quart.) This "self-enrichment" provides a 25% increase in protein, calcium and B-vitamins with no increase in liquid bulk.

25% "self-enriched" Carnation Instant also provides a more familiar heavier texture and richer flavor, well-liked by patients who are accustomed to drinking whole milk.

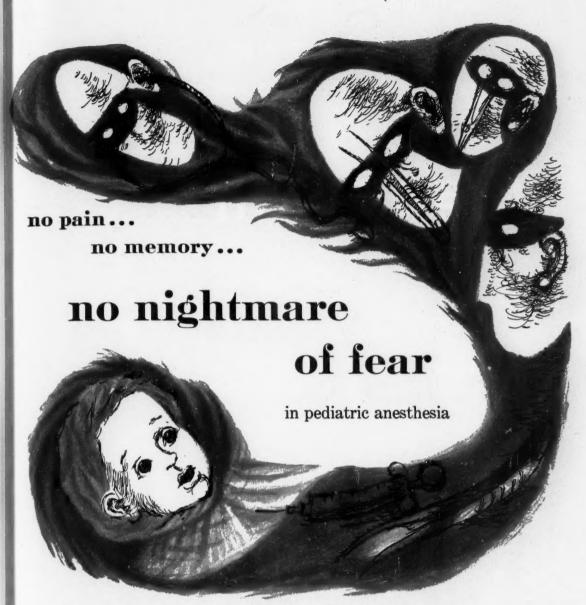
WHEN PROTEIN NEEDS ARE HIGH,

the physician may recommend the addition of 1½ cups Carnation crystals to each quart of whole milk. This doubles the protein, calcium and B-vitamin content.

The use of Carnation Instant in whole milk is of value when some fat is advisable but liquids should be restricted...and is also useful in increasing the protein in geriatric or convalescent diet without increasing fat or liquid bulk.

Other advantages of the Carnation exclusive Crystal Form Fresh milk flavor, delicious for drinking. Mixes instantly in ice-cold water. Does not cake or harden in the package. No special recipes needed. Economical, available everywhere.

Jul



When you choose Pentothal Sodium by rectum as the basal anesthetic, or as the sole agent in minor procedures, you spare your young patients an unnecessary ordeal of fear and anguish. With Pentothal Sodium administered rectally, the child goes to sleep pleasantly in his own bed . . . and awakens there after surgery with complete amnesia of the events between. Events, that in his sensitive mind

might cause lingering post-operative anxieties, creating new behavior problems for his parents.

And because Rectal PENTOTHAL reduces the dosage of inhalation and supplementary agents, after-effects are markedly lessened. It offers a notably safe, simple and humane approach to pediatric anesthesia. Do you have the literature?

PENTOTHAL Sodium

(Thiopental Sodium, Abbott)



ynec

magnified potency
with Meti-steroid
effectiveness in allergic
and inflammatory dermatoses

new

Meti-Derm cream 0.5%

with METICORTELONE, original brand of prednisolone

· approximately

twice the per milligram

anti-inflammatory activity

of topical hydrocortisone

- · cosmetically acceptable
 - · water-washable

for effective local relief of allergic (atopic and contact) dermatoses, nonspecific anogenital pruritus.

formula: Each gram of water-washable METI-DERM Cream contains 5 mg. (0:5%) of prednisolone, free alcohol, in a cosmetically acceptable base.

packaging: METI-DERM Cream, 0.5%; 10 Gm. tube

METI-DERM,* brand of prednisolone topical METICORTELONE,* brand of prednisolone.

...and adding dual control
to Meti-steroid skin therapy—
protection
against infection

new

Meti-Derm ointment

with Neomycin



enhanced effectiveness

in allergic, inflammatory

dermatoses when

minor infection

is present

or anticipated

neomycin in addition to prednisolone, free alcohol —for protective coverage against virtually all pathogenic skin bacteria with a well-tolerated, topical antibiotic.

formula: Each gram of water-washable METI-DERM Ointment with Neomycin contains 5 mg. (0.5%) prednisolone, and 5 mg. (0.5%) neomycin sulfate equivalent to 3.5 mg. neomycin base.

packaging: METI-DERM Ointment with Neomycin, 10 Gm. tube.



Schering





new...simple...effective...topical therapy

Clinical evidence shows Sterisil Vaginal Gel to be highly effective not only against Trichomonas and Monilia, but against the newly discovered pathogen *Hemophilus vaginalis* (now believed to be the etiologic organism most frequently responsible for so-called "nonspecific" vaginitis and leukorrhea).*

High tissue affinity of Sterisil assures prolonged antiseptic action; vaginal secretions are less likely to remove Sterisil from the site of application. Sterisil is also more convenient for the patient. Fewer applications are required for successful treatment. Acceptable to patients, Sterisil Vaginal Gel is easily applied, won't leak or stain, requires no pad. Signs of local or systemic toxicity or sensitization have not been reported.

Dosage: One application every other night until a total of 6 has been reached. This treatment may be repeated if necessary.

Supplied in $1\frac{1}{2}$ oz. tube with 6 disposable applicators. Instructions for use are included with each package.

*Gardner, H. L., and Dukes, C. D.: Am. J. Obst. & Gynec. 69:962 (May) 1955.

STERISIL VAGINAL GEL

WARNER-CHILCOTT

Safety First

in control of Nausea of Pregnancy

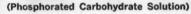
The first thought of every physician during the prenatal period is the safety of the patient.

The first choice of the physician for an agent to control nausea and vomiting will be EMETROL® when he considers the following advantages:

- 1. EMETROL does not contain barbiturates, bromides, antihistamine compounds, or any other drugs likely to induce untoward effects.
- 2. EMETROL has been shown to be effective in nausea and vomiting in controlled clinical studies. 1-3
- 3. EMETROL is so palatable that most patients will take it readily.

4. EMETROL works quickly, often bringing relief with the first dose.

SAFE



- Crunden, A. B., Jr., and Davis, W. A.: Am. J. Obst. & Gynec. 65:311, 1953.
- Bradley, J. E., et al.: J. Pediat. 38:41, 1951.
- Tebrock, H. E., and Fisher, M. M.: M. Times 82:271, 1954.

Kinney

KINNEY & COMPANY, INC. COLUMBUS, INDIANA

July, 1956

iitis

Page 31



Her most important asset is her health. > With health, she is happy, relaxed and capable of serving her family and community. > Today, parents turn to their family physician for advice on scientific methods of child-spacing, for it is he who recognizes the medical necessity for such advice . . . guides her . . . and earns her

gratitude. Without this attention from her doctor, in whom she places her confidence, her family goals would not be easily obtained. It's the incomparable knowledge, skill and experience of her doctor...and doctors everywhere...whose judgment is to recommend for their patients' health and happiness.

AVAILABLE AT ALL LEADING PHARMACIES' . KOROMEX JELLY, CREAM AND DIAPHRAGM COMPACT HOLLAND-RANTOS COMPANY, INC. . 145 HUDSON STREET . NEW YORK 13, N. Y. Page 32

Am. J. Obst. & Gynec.

95% FETAL SALVAGE

with HESPER-C



- 1 Red blood cells escaping from a capillary under abnormal conditions of capillary fragility.
- 1
 - 2 Bleeding into the decidua basalis results from increased permeability of the uterine capillaries. The decidua then splits; a decidual hematoma is formed which leads to premature separation of the normally implanted placents.



the original synergistic nutritional supplement for capillary fragility, is recommended as an integral part of any regimen for fetal salvage.¹ Maintaining capillary integrity during the critical months guards against abruptio placentae.² In 100 patients whose 420 previous pregnancies resulted in 95% fetal wastage, the addition of HESPER-C to current therapy completely reversed the figure and resulted in 95% fetal salvage.³

Remember Rx HESPER-C along with your usual therapy—it makes the difference.

Maintain the integrity of the capillaries throughout pregnancy.

on your

prescription

only





HESPER-C provides hesperidin concentrate, 100 mg., and ascorbic acid, 100 mg., per capsule and per teaspoonful (5 ml.). DOSAGE: 6 capsules or teaspoonfuls or more per day for the first week. Then 4 capsules or teaspoonfuls daily. SUPPLIED: Liquid in bottles of 4 oz. and 12 oz. Capsules in bottles of 100 and 1000.

REFERENCES: 1. Dill, L. V.: Med. Ann. of D. of C., 23:667, 1954. 2. Greenblatt, R. B.: Obst. and Gyn., 2:530, 1953. 3. Javert, C. T.: Obst. and Gyn., 3:420, 1954.

The film "CLINICAL ENZYMOLOGY" is now available for showing at medical meetings upon your request. And be sure to watch for the MED-AUDIOGRAPHS, a series of recorded clinical discussions.



PRODUCTS OF ORIGINAL RESEARCE

NATIONAL

r, in

ould

lwor

ctors

their ex

PACT N. Y.

nec.

NATIONAL

NATIONAL

NATIONAL

NATIONA

NATIONAL

THE NATIONAL DRUG COMPANY PHILADELPHIA 44, PA.

The CLASSICAL Vaginal Therapeuti



UNIQUE WITH 9-AMINOACRIDINE, the nonirritating, broad-spectrum, stable bactericidal agent. Effective where organisms have become resistant to other drugs.

AVC Improved has been accepted, and in ever-expanding use for over 12 years, as the most comprehensive therapy in:

Trichomonal Leukorrheas • Monilial and Nonspecific Vaginitis • Cervicitis • Postpartum Hygiene • Pre- and Postcauterization, Coagulation, Conization and other Vaginal Surgery

AVC Improved provides: Broad-spectrum, sustained vaginal pathogen killing power because the remarkable synergism of 9-aminoacridine and sulfanilamide effects the actual destruction of the inhibitors of maximum bactericidal action. Surface-active, spreading, penetrating agent; buffered vaginal pH; nutrient for normal vaginal flora; mucus digestion; immediate relief of odor and itching; restoration of vaginal mucosa, by actively promoting tissue repair and granulation.

AVC Improved is a cream containing 0.2% 9-Amino-acridine Hydrochloride, 15% Sulfanilamide, 2% Allantoin, in a water-miscible base buffered to approximately pH 4.5.



SUPPLIED: 4 oz. tubes or without applicator. MINISTRATION: An plicatorful of AVC Improshould be introduced high the vagina twice daily, arising and at bedtime.

PRODUCTS OF ORIGINAL RESEARCE

THE NATIONAL DRUG COMPANY PHILADELPHIA 44,



Newest in vitamin therapy Vitamins as nature intended . . .

HOMOGENIZED VITAMINS

For the first time, all the advantages of multivitamin drops are available in a tablet. By a unique process, the vitamins are homogenized, then fused into a solid, highly palatable form.

As a result of this minute subdivision, the vitamins are absorbed and utilized much more efficiently than those in the usual compressed tablet or elastic capsule.

- Better absorbed and utilized
- Pleasant, candy-like flavor
- No regurgitation, no "fishy burp"
 May be chewed, swallowed, or dissolved in the mouth

Three formulas:

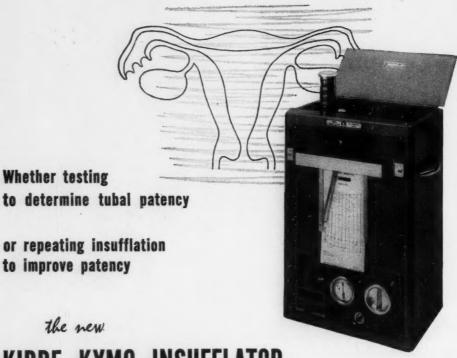
Prenatal **Pediatric Therapeutic**

The S.E. MASSENGILL COMPANY Bristol, Tennessee

New York • Kansas City • San Francisco

ubes

tor.



KIDDE KYMO INSUFFLATOR

provides precise records of pressure variations for hospital files or referral patients

Oscillation patterns are easy to read and compare from rectangular graphs. Accuracy is assured by positive electrical control of graph during insufflation.

SAFE AND SIMPLE The Kidde Kymo Insufflator is charged in seconds from a disposable, hermetically sealed cartridge of CO₂. Automatic controls limit the quantity of gas released into the tubes to 100 cc. Maximum pressure is limited by gravity controls to 200 mm. Hg. Rate of flow for each patient is regulated by a single finger-tip control and constantly revealed by the Flow Meter. Pure, filtered carbon dioxide is promptly absorbed by the patient—with no risk of emboli.

For instilling contrast media for salpingography, the Kidde Opaque Oil Attachment is available.

Ask your dealer to demonstrate or write for information to

KIDDE MANUFACTURING COMPANY

Bloomfield, New Jersey Kidde, Trademark Reg. U.S. Pat. Off.

The new model
KIDDE KYMO INSUFFLATOR
is compactly designed
and portable.
Weight-25 lbs.
Size-8" x 11" x 17"

The most completely safe instrument for tubal insufflation available



help assure optimal nutrition during gestation...throughout lactation

NATABEC KAPSEALS.

vitamin-mineral combination

You can help assure optimal nutrition in your patients during pregnancy and lactation by supplementing their diet with NATABEC Kapseals. Designed to improve intake of important vitamins and minerals at these times of increased nutritional need, NATABEC Kapseals, taken regularly, help avoid complications and aid in safeguarding the health of both mother and child.

dosage: As a dietary supplement during pregnancy and lactation, one or more Kapseals daily. NATABEC Kapseals are available in bottles of 100 and 1,000.



PARKE, DAVIS & COMPANY DETROIT, MICHIGAN



weeks?

months?

years?

Improve the prognosis in fractures with "Premarin" with Methyltestosterone

Healing of fractures is often delayed because impairment of osteoblastic actividue to declining sex hormone function causes the bone matrix to atrophy.

Older patients with fractures, particularly of the hip, respond well to combine estrogen-androgen therapy. The prognosis for bone recalcification is good provide treatment is continued for extended periods.*

*Reifenstein, E. C., Jr., in Harrison, T. R.: Principles of Internal Medicine, ed. 2, New York, 1 Blakiston Company, Inc., 1954, chap. 98, pp. 702, 703.

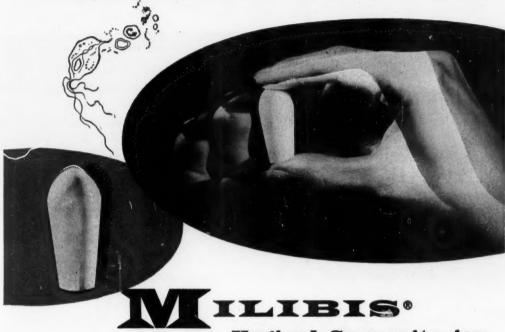
"PREMARIN" with METHYLTESTOSTERONE

Excellent preparation for estrogen-androgen therapy

Ayerst Laboratories . New York, N. Y. . Montreal, Canada



New Effective ... for WAGINITIS:



Vaginal Suppositories

-soft and pliant as a tampon-white, odorless, non-staining-the suppositories bring new ease and new effectiveness to treatment of vaginitis.

ELIMINATE SMEAR EXAMINATIONS*

Milibis vaginal suppositories are effective in trichomonad, Candida (monilia) as well as mixed and bacterial infections-thus laboratory identification of the offending organism is unnecessary.

THERAPEUTIC REGIMEN IS SHORT AND SIMPLE

A total of only 10 suppositories (one inserted every other night) has given a remarkable rate of cure of over 90 per cent in two large series of cases. Milibis vaginal suppositories are easily inserted high into the vagina and form a tenacious film which coats the cervix and rugae, killing pathogens on contact. Non-staining, well tolerated.

*Except when gonorrheal infection is suspected.



Milibis (brand of glycobiarsol), trademark reg. U.S. Pat. Off.



SUPPLIED: BOXES OF 10

k Gyn July, 1956

s?

activi

mbin

rovid

York, T

Page 37

"...THE

MOST

EFFECTIVE

HEMATINIC..."*



LI

The convincing evidence supporting the unique and advanced concept of cobalt-iron therapy in anemia is based on RONCOVITE research.

Roncovite is the only clinically proved preparation supplying cobalt in the therapeutic levels essential for the optimal hematologic response in anemia. The presence of cobalt as a specific bone marrow stimulant improves the utilization of iron and makes Roncovite totally different from any other hematinic preparation.

The safety and potency of Roncovite has been repeatedly confirmed.

Your own results will show why "The bibliography specifies RONCOVITE."

THE BIBLIOGRAPHY SPECIFIES



RONCOVITE®

-THE ORIGINAL CLINICALLY PROVED COBALT-IRON PRODUCT-

Holly, R.G.: Anemia in Pregnancy, Obst. & Gynec. 5:562 (April) 1955.

Hill, J.M., et al.: Cobalt Therapy in Anemia, Texas J. Med. 51:686 (Oct.) 1955.

Rohn, R.J.; Bond, W.H., and Klotz, L.J.: The Effect of Cobalt-Iron Therapy in Iron-Deficiency Anemia in Infants, J. Indiana M.A. 46: 1253 (1953).

Holly, R.G.: Anemia in Pregnancy, Paper delivered before Amer. Congress of Obstetrics and Gynecology (Dec.) 1954.

* Holly, R.G.: The Value of Iron Therapy in Pregnancy, Journal Lancet 74:211 (June) 1954.

Quilligan, J.J., Jr.: Effect of a Cobalt-Iron Mixture on the Anemia of Prematurity, Texas J. Med. 50: 294 (May) 1954.

Hamilton, H.G.: The Use of Cobalt and Iron in the Prevention of Anemia of Pregnancy. Paper delivered before the South.Med. Assn.

Rohn, R.J., and Bond, W.H.: Observations on Some Hematological Effects of Cobalt-Iron Mixtures, Journal Lancet **73**:317 (Aug.) 1953.

Holly, R.G.: Studies on Iron and Cobalt Metabolism, J.A.M.A. 158: 1349 (Aug.13) 1955.

Jaimet, C.H., and Thode, H.G.: Thyroid Function Studies on Children Receiving Cobalt Therapy, J.A.M.A. 158:1353 (Aug. 13) 1955.

Klinck, G.H.: Thyroid Hyperplasia in Young Children, J.A.M.A. 158:1347 (Aug. 13) 1955.

Tevetoglu, F.: The Treatment of Common Anemias in Infancy and Childhood with a Cobalt-Iron Mixture. Driscoll Foundation Children's Hosp., Corpus Christi, Texas (April) 1956.

Ausman, D.C.: Cobalt-Iron Therapy in the Treatment of Some Common Anemias Seen in General Practice, in press.

LLOYD!

BROTHERS, INC.

Cincinnati 3, Ohio

no other suppository can do more to bring

Sund South State of the State o

sustained comfort to your anorectal patients than

DESITIN

hemorrhoidal
SUPPOSITORIES

with cod liver oil

DESITIN SUPPOSITORIES afford rapid relief in hemorrhoids (non-surgical). Norwegian cod liver oil (rich in vitamins A and D and unsaturated fatty acids) helps promote healing. They do not contain styptics, local contains and the statement of the

anesthetics, or narcotics and therefore do not mask serious rectal disease In boxes of 12

samples are available from

DESITIN CHEMICAL COMPAN

Providence, R.I

Am. J. Obst. & Gym July

soothes •

protects •

lubricates •

eases pain •

relieves itching •

decongests •



SURGILAR KEEPS

BROKEN GLASS OUT OF O.R. Surgeons report
new loose coil packaging delivers a stronger,
more flexible strand. Nurses report 3315% less handling
time—surgeons get more nurse-power! SURGILAR
eliminates worries and waste from cut gloves
and hands, damaged linens and breakage.
SURGILAR requires 50% less storage space—
costs no more than tubes!

Improve patient care with D & G's hospital-tested

STERILE PACK SUR GICAL GUT

D & G hospital - tested

Ask your D & G
representative for
more information or
write Director of
Professional
Relations

packaging makes the difference

DAVIS & GECK INC.

A HNIT OF EWERICAN CYANAMID COMPAN

DANBURY TO CONNECTION

July, 1956

(rich

helps

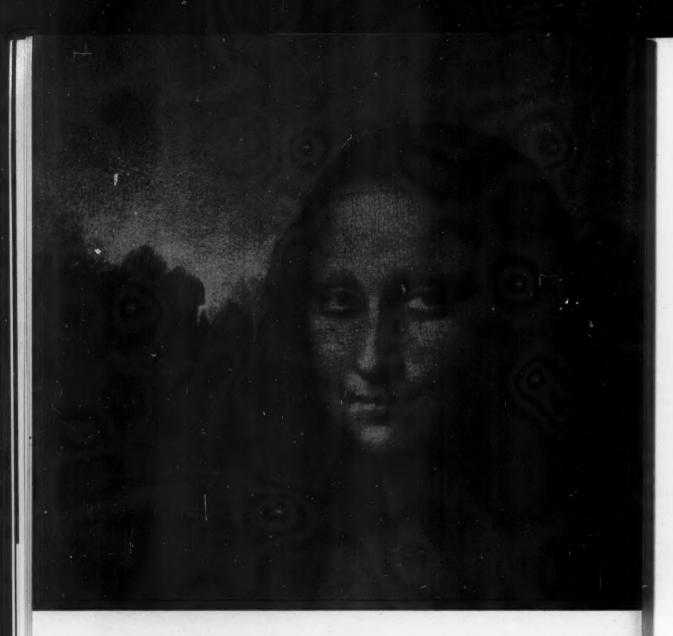
local refore sease

of 12

PANI

, R.I.

Page 41



A SMILE AGAIN IN JUST 12 DAYS WITH TIME-SAVING TRIV

the MODERN treatment for all 3 types of vaginitis

TRIVA effectively annihilates vaginal microorganisms, restores mucos integrity and accelerates healing for rapid recovery.

Non-irritant, non-toxic, non-staining, TRIVA is a safe vaginal douched even during pregnancy. Effective in any pH medium. Most cases of the chomonal, monilial and non-specific vaginitis become asymptomatic and organism free in 6 to 12 days. For complete data see Physicians' Des Reference, 1956, page 427.

AVAILABLE AT ALL PHARMACIES, in convenient packages of 24 individual 3 Gm. packets, each containing 35% Alkyl Aryl sulfonate, (surface-acting germicidal and detergent), 0.33% Disodium ethylene bis-iminodiacette (chelating agent), 53% Sodium sulfate, 2% Oxyquinoline sulfate (but tericide, protozoacide) and 9.67% dispersant.

Full treatment package and literature on request.



BOYLE & COMPANY · Bell Gardens, California

Jul



Yes . . .

desPLEX

to prevent ABORTION, MISCARR

PREMATURE LABOR

recommended for routine proph in ALL pregnancies . .

96 per cent live delivery with desPLEX in one series of 1200 patients4-- bigger and stronger babies, too.cf. 1

No gastric or other side effects with desPLEX

- in either high or low dosage 3,4,5

(Each desPLEX tablet starts with 25 mg. of diethylstilbestrol, U.S.P., which is then ultramicronized to smooth and accelerate absorption and activity. A portion of this ultramicronized diethylstilbestrol is even included in the tablet coating to assure prompt help in emergencies. desPLEX tablets also contain vitamin C and certain members of the vitamin B complex to aid detoxification in pregnancy and the effectuation of estrogen.)

For further data and a generous trial supply of desPLEX, write to:

Medical Director

REFERENCES

- Canario, E. M., et al.: Am. J. Obst. & Gynec. 65:1298, 1953.
 Gitman, L., and Koplowitz, A.: N. Y. St. J. Med. 50:2823, 1950.
 Karnaky, K. J.: South. M. J. 45:1166, 1952.
 Peña, E. F.: Med. Times 82:921, 1954; Am. J. Surg. 87:95, 1954.
 Ross, J. W.: J. Nat. M. A. 43:20, 1951; 45:223, 1953.

GRANT CHEMICAL COMPANY, INC., Brooklyn 26, N.Y.

VIS

ucos

che.

of tri

ic an

Des

ividu actin aceta ? (ba BREAK THE RE-INFECTION CYCLE

OF

CONJUGAL (() () PARTNERS

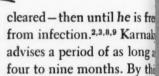
IN VAGINAL TRICHOMONIASIS

Vacinal trichomoniasis, common in women, is now recognized as a disease whose causative agent also infects the male. The number of women harboring trichomonads "...has recently been put as high as 24%."

Not uncommon in husbands – Evidence shows trichomonads can be found in from 5 to 15 per cent of the male population, 2,3 or even more. Freed reported that 28.5 per cent of men in his studies were carriers. In Feo's investigation, "the incidence of non-specific urethritis cases which may be attributable to Trichomonas vaginalis was 36.9 per cent." Karnaky found the parasites in the urethra and prostate or under the prepuce in 38 among 150 husbands with infected wives.

The symptomless vector—"... many patients with trichomonas vaginitis are infected and reinfected by coitus..." with husbands who may be highly infective without showing clinical symptoms. Infected wives can in turn reinfect husbands.

Protection against re-infection—To break the cycle of re-infection, authorities agree that the husband should use a condom regularly during coitus while the wife is under treatment and until it is established that her infection has



time the husband's infection will usually di out of its own accord.⁸ Davis states: "Obviously the man who has a chronic trichomona infection...will continue to reinfect his wife unless he wears a sheath during coitus." ⁹

Prescription of condoms—Seek the aid of the husband when you treat the wife. "How The Husband Can Help," a booklet for patient explains his role in the control of trichomoniasis. Copies are available upon request. Us this booklet to gain his cooperation, make explanations easier, save your time.

In prescribing condoms, be specific. Take advantage of Schmid product improvements the win acceptance of your treatment plan. If there is anxiety that the condom might retain sensation, specify XXXX (FOUREX) skins Made from the cecum of the lamb, tissue smooth and pre-moistened, they do not dusensory effect. If there is a preference for a rubber condom, specify the superior RAMSES prophylactics. These are different, transparent very thin yet strong, of natural gum rubber

References: 1. McEntegart, M. G.: J. Clin. Path. 5:27 (Aug.) 1952. 2. Draper, J. W.: Internat. Rec. Med. 168:58 (Sept.) 1955. 3. Bernstine, J. B., and Rakoff, A. E.: Vapnal Infections, Infestations and Discharges, New York, Ib Blakiston Co., 1953. 4. Freed, L. F.: South African M., 22:223 (Mar. 27) 1948. 5. Feo, L. G.: Am. J. Trop. Me 24:195 (May) 1944. 6. Karnaky, K. J.: Urol. & Cutan. Re 42:812 (Nov.) 1938. 7. Lanceley, F.: Brit. J. Ven. D. 29:213 (Dec.) 1953. 8. Karnaky, K. J.: J.A.M.A. 155:81 (June 26) 1954. 9. Davis, C. H. (Ed.): Gynecology Obstetrics (revision), Hagerstown, W. F. Prior, 1955, vi. 3, chap. 7, pp. 23-33.

JULIUS SCHMID, INC., prophylactics division 423 West 55th Street, New York 19, N. Y.

Jul

TEN-EIGHTY SURGICAL OPERATING TABLE

The unexcelled versatility of the American ten-eighty surgical operating table is measurably increased by new and specialized accessories which facilitate the complete accessories modern operative procedures.

A M E R I C A N STERILIZER

Erie · Pennsylvania

Your copy of Accessory Brochure C-183 is available upon request.



Narrow Table Attachment for infant surgery and head and neck surgery permits surgeon ideal proximity to operative site.



Illustrating use of Arm Support, Headrest and Restraint Strap appropriate for a neurosurgical procedure in the upright position.



Thoracic Frame for prone positioning provides unobstructed access to the operative site, minimum shock to patient and progressive posturing during procedure.

is fre

ong a
By thi

Obvi mona is wife

w The

tient omoni

t. Us mak

ike ad

ents to lan. I retan

skins

tissue ot dul a rub ISES parent

n. 5:27 168:56 C.: Vapork, The an M. Jop. Med tan. Reven. Dis 155:87

logy and

Gynn

American Journal of Obstetrics and Gynecology

Editors: HOWARD C. TAYLOR, JR. 622 West 168th St., New York 32, N. Y.

AND

WILLIAM J. DIECKMANN 5841 Maryland Ave., Chicago 37, Ill.

Published by The C. V. Mosby Company, 3207 Washington Blvd. St. Louis 3, Mo.

Entered at the Post Office at St. Louis, Mo., as Second-Class Matter.

Published Monthly. Subscriptions may begin at any time.

Editorial Communications

Original Contributions.—Contributions, letters, and all other communications relating to the editorial management of the Journal should be sent to Dr. Howard C. Taylor, Jr., 622 West 168th St., New York 32, N. Y., or to Dr. William J. Dieckmann, 5841 Maryland Ave., Chicago 37, Ill.

All articles published in this Journal must be contributed to it exclusively. If subsequently printed elsewhere (except in a volume of Society Transactions) due credit shall be given for original publication. The Editors rely on all contributions conforming strictly to this rule.

be given for original publication. The Editors rely on all contributions combining strictly to this rule.

Members of the Advisory Editorial Board may be consulted by the Editors upon suitability of papers submitted for publication.

It is assumed by the Editors that articles emanating from a particular institution are submitted with the approval of the requisite authority.

Neither the Editors nor the publishers accept responsibility for the views and statements of authors as published in their "Original Communications."

Manuscripts.—Manuscripts should be typewritten on one side of the paper only, with double spacing and liberal margins. References should be placed at the end of the article and should conform to the style of the Quarterly Cumulative Index Medicus: viz., name of author, name of periodical, volume, page, and year. Illustrations accompanying manuscripts should be numbered, provided with suitable legends, and marked lightly on the back with the author's name. Authors should indicate on the manuscript the approximate position of tables and text figures.

Illustrations.—A reasonable number of halftone illustrations will be reproduced free of cost to the author, but special arrangements must be made with the editors for color plates, elaborate tables, or extra illustrations. Copy for zinc cuts (such as pen drawings and charts) must be drawn and lettered in India ink or black typewriter ribbon (when the typewriter is used). Only good glossy photographic prints should be supplied for halftone work; original drawings, not photographs of them, should accompany the manuscript.

Announcements.—Announcements of meetings must be received by the Editors at least 2½ months before the time of the meeting.

Exchanges.—Contributions, letters, exchanges, reprints, and all other communications relating to the Abstract or Review Department of the Journal should be sent to Dr. Louis M. Hellman, State University of New York, College of Medicine, 451 Clarkson Ave., Brooklyn 3, N. Y.

Reviews of Books.—Books and monographs, native and foreign, on obstetrics, gynecology, and abdominal surgery will be reviewed according to their merits and the space at disposal. Send books to Dr. Louis M. Hellman, State University of New York, College of Medicine, 451 Clarkson Ave., Brooklyn 3, N. Y.

Reprints.—Reprints of articles must be ordered from the publishers, The C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, Mo., who will send their schedule of prices. Individual reprints of an article must be obtained through the author.

Business Communications

Business Communications.—All communications in regard to advertising, subscriptions, changes of address, etc., should be addressed to the publishers, The C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, Mo.

Subscription Rates.—United States and its Possessions \$15.00, Students \$7.50; Canada, Latin-America, and Spain \$16.00, Students \$8.50; Other Countries \$17.50, Students \$10.00. Single copies, \$2.50 postpaid. Remittances for subscriptions should be made by check, draft, post office or express money order, payable to this Journal.

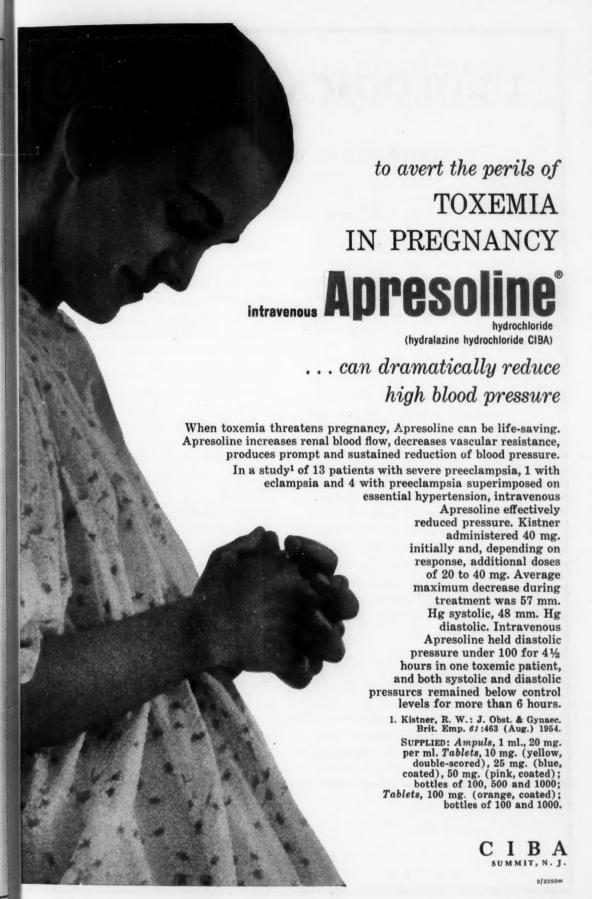
Publication Order.—The monthly issues of this Journal form two semiannual volumes; the index is in the last issue of the volume—in the June and December issues.

Change of Address Notice.—Six weeks' notice is required to effect a change of address. Kindly give the exact name under which a subscription is entered, and the full form of both old and new addresses, including the post office zone number.

Advertisements.—Only products of known scientific value will be given space. Forms close first day of month preceding date of issue. Advertising rates and page sizes will be given on application.

Bound Volumes.—Publishers' Authorized Bindery Service, 308 West Randolph Street, Chicago 6, Illinois, will quote prices for binding complete volumes in permanent buck-

July



July, 1956

Gyne

Page 47

UROLOGICAL SURGERY

by

AUSTIN INGRAM DODSON, M.D., F.A.C.S.

Richmond, Virginia

3rd (1956) Edition

868 pages, 650 illustrations

\$20.00

Lat

(Absti

stetric

pend

oozii

been the u

H

salic

com

It ap

acter

It ha

does

affec

neith The

of w Salid obsta

Bris

Th

Here is a book covering the entire subject of Urological Surgery. Where improvements in former procedures have been made, they are included. New operations, when considered to advantage, are added. A new chapter on Adrenal Surgery has been added.

Three chapters occurring in the two previous editions have been eliminated. The problem of Acid-Base Balance and Fluid Administration has become too broad a subject to be treated adequately in a single chapter. A brief discussion of this subject as well as Blood Transfusions and the Treatment of Shock is included in the chapter on Preoperative and Postoperative Care. Radiation therapy, with the addition of new radioactive substances, has become too broad a subject to be adequately discussed in the space available. By eliminating these chapters surgical procedures and illustrations have been added.

The chapter on surgical diseases of the adrenal glands and the section on ure-

terosigmoidostomy, Chapter XXIII, have been rewritten by Dr. A. I. Dodson, Jr. Chapter XXXII in the second edition—Neurogenic Diseases of the Bladder—has been replaced by a chapter on Surgical Treatment of Urinary Tract Dysfunction Caused by Disease or Injury of the Nervous System. This chapter by Dr. Robert C. Bunts deals chiefly with the urological rehabilitation of the paraplegic patient.

The section on Perineal Prostatectomy has been rewritten by Dr. Albert E. Goldstein with new illustrations. In Chapter XXXVI more attention is given the problem of stress incontinence, and operations found beneficial in the author's experience have been added. Some changes have been made in many of the remaining chapters, consisting chiefly in the addition of surgical procedures or illustrations. A separate chapter has been added dealing with postoperative incontinence of the male.

THE C. V. MOSBY COMPANY	DATE
3207 Washington Blvd., St. Louis 3, Missouri	
Gentlemen: Send me the Third (1956) Edition of Doc Price, \$20.00.	dson "UROLOGICAL SURGERY."
DR,STREET	
CITYSTATE	B
	AJOG-7-50

Latest clinical report on Adrenosem® Salicylate

(brand of carbazochrome salicylate)

The Use of the
Systemic Hemostat
Carbazochrome
Salicylate

J. C. Bacala, M.D.

(Abstracted from the Western Journal of Surgery, Obstetrics, and Gynecology, 64:88 (1956)

The author emphasizes the need for dependable chemical control of bleeding and oozing, and reviews the methods that have been tried to attain hemostasis, including the use of vitamin K and bioflavonoids.

He gives the history of carbazochrome salicylate and describes the clinical work completed to demonstrate its effectiveness. It appears to be specific for conditions characterized by increased capillary permeability. It has no effect on large blood vessels; it does not alter blood components; it does not affect blood pressure or cardiac rate. It has neither vasoconstrictor or vasodilator action. The drug has no known contraindications.

He reviews 1051 cases from the files of St. Anthony Hospital, Louisville, Kentucky, of which 330 were treated with Adrenosem Salicylate. 317 were surgical cases and 13 obstetric-gynecological conditions. The treat-

ment was given for symptomatic relief, and as a clinical recourse for patient safety.

In 1015 tonsillectomy patients the following results were noted: There was bleeding in 85 (19.8%) of 429 patients who received no medication. Patients who received a compound of oxalic and malonic acids numbered 115. Of these 16 (14%), developed bleeding. Of 248 patients receiving vitamin K preparations, 47 (19%) had postoperative hemorrhage. 233 patients received Adrenosem Salicylate. Of this group, only 16 (7%) had bleeding.

In other surgical conditions, Adrenosem was used successfully in gastrointestinal bleeding, cataract extraction, incisional seepage, and transurethral prostatectomy. It was also effective in 12 cases of epistaxis.

In the field of obstetrics and gynecology, Adrenosem controlled bleeding in menometrorrhagia, hymeneal laceration, cervical ooze, antepartum and postpartum bleeding, threatened abortion, and in two cases of surgery during pregnancy.

The author points out that in pregnancy, seepage bleeding occurs more because of capillary permeability, and in spite of increased coagulability. Here, Adrenosem becomes specific for strengthening capillary resistance.

Many of the observations in this study, however, involved bleeding incident to trauma of incision, retraction, dissection, tearing and stretching. In these conditions, he reasons that Adrenosem causes hemostasis by its effect on the capillary intercellular cement substance so that the cells draw closer together, and the ends of the capillaries constrict, causing a "self-clamping" mechanism.

The S. E. MASSENGILL company

FILMS showing the uses of

drenose m Salicylate

(brand of carbazochrome salicylate)

in the control of bleeding

Films in color, demonstrating the uses of Adrenosem Salicylate* in surgery, are now available for showing to hospitals, medical societies and group meetings. Write to Film Division, S. E. Massengill Co., Bristol, Tennessee.

Send for comprehensive illustrated brochure describing the action and uses of this unique systemic hemostat.

INDICATED preoperatively and postoperatively to control bleeding associated with:

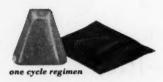
Tonsillectomy, adenoidectomy and nasopharynx surgery
Prostatic and bladder surgery
Dental surgery
Chest surgery and chronic pulmonary bleeding
Uterine bleeding and postpartum hemorrhage
Also: Idiopathic purpura, retinal hemorrhage, familial te
angiectasis, epistaxis, hematuria

Supplied in ampuls, oral tablets and as a syrup.

The S. E. MASSENGILL company BRISTOL TENNESSEE - NEW YORK - KANSAS CITY - SAN FRANCISCO

*U. S. Pat. 258185

July



Vaginal trichomoniasis: lasting cure for 93.8%

Within 72 hours, local irritation no longer troubled this patient. Relief resulted from thorough powder insufflation by her doctor and her use of suppositories at home.

- after clinical study of 48 active cases, Schwartz reported 93.8% were symptom-free in 3 days; 97.9% showed no motile trichomonads on smear in 7 days; 93.8% had no recurrence 1 to 3 months after treatment through one menstrual cycle*
- advantages: contains a specific, trichomonacidal nitrofuran. Kills many secondary invaders but permits Döderlein's bacillus to exist. Effective in blood, pus and vaginal debris
- office treatment: insufflate Trico-Furon Vaginal Powder twice the first week and once a week thereafter
- home treatment: first week—the patient inserts one Tricofuron Vaginal Suppository each morning and one each night at bedtime. Thereafter: one a day—a second if needed—to maintain trichomonacidal action



TRICOFURON

EATON LABORATORIES

Norwich



New York

NITROFURANS a new class of antimicrobials neither antibiotics nor sulfonamides

VAGINAL SUPPOSITORIES AND POWDER

Suppositories: 0.25% Furoxone® (brand of fürazolidone) in a water-miscible base of Carbowax and 20 dendro palmitic acid. Sealed in green foil, box of 12.

Powder: 0.1% Furoxone in an acidic powder base of lactose, dextrose, citric acid and a silicate. Bottle of 30 Gm.

*Schwartz, J.: Obst. Gyn. N. Y. 7:312, 1956.

JEANES HUSPITAL

Fox Chase Page 49
Philadelphia 11, Pa

July, 1956

185

"...the oral
administration of a
molybdenum ferrous
sulfate compound (Mol-Iron)
effectively treated 95 per cent
of a group of 66 patients
with iron deficiency anemia
of pregnancy."1

"in none

(of the patients treated)

was it necessary

to suspend treatment

because of

intolerance."2



mol-iron tablets

MOLYBDENIZED FERROUS SULFATE

1. Lund, C.J.: Am. J. Obst. & Gynec, 62:947 (Nav.) 1951

2. Chesley, R.F., and Annitto, J.E.: Bull. Marg. Hague Mat. Hosp. 1:68 (Sept.) 1948. WHITE LABORATORIES, INC., KENILWORTH, N.J. Other Convenient Dosage Forms:
Mol-Iron Liquid
Mol-Iron Drops

Complete literature on request



Rational dietary
supplementation
through pregnancy
-minimal risk at term

GESTATABS®

The Mol-Iron® Prenatal Supplement

Provides

Just 2 for 2

Nutritional Protection

for both mother and child

- Phosphorus-free calcium to reduce chances of leg cramps
- Vitamin K to protect against neonatal prothrombin deficiency
- Mol-Iron clinically proved to be far better tolerated ... the most effective form of iron therapy.

Two Tablets Daily Supply:

Vitamin A 6,000 U. S. P. Units
Vitamin D
Vitamin K (menadione) 2 mg.
Vitamin B ₁₂ Activity Equivalent*
Folic Acid 1 mg.
Ascorbic Acid 100 mg.
Thiamine mononitrate 3 mg.
Riboflavin 5 mg.
Pyridoxine hydrochloride
Calcium pantothenate 10 mg.
Nicotinamide 30 mg.
Mol-Iron
Ferrous sulfate 120 mg.
Molybdenum oxide 1.8 mg.
Calcium (elemental)** 380 mg.

*As in Streptomyces fermentation extractives.
**From calcium gluconate and calcium carbonate.

Conveniently packaged in bottles of 60 tablets (one month's supply)

And when iron is the dominant need

MOL-IRON with Calcium and Vitamin D

therapeutic amounts of iron plus supplementary Vitamin D and phosphorus-free calcium in small easily swallowed tablets.

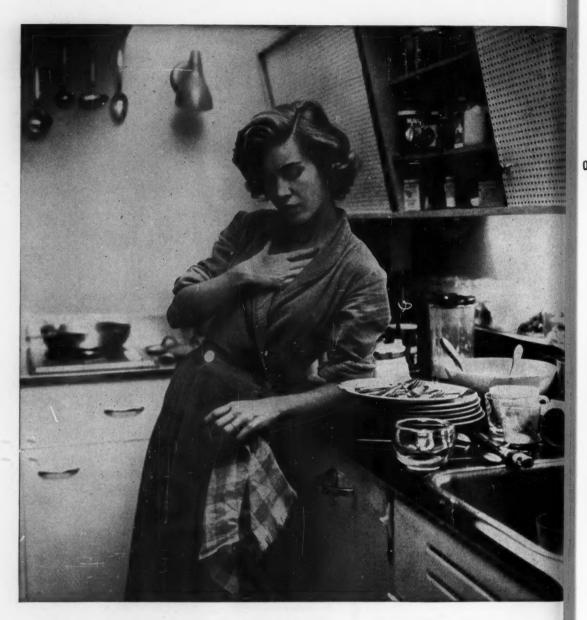
¹Complete bibliography on request.

Whiteis

ns:

st

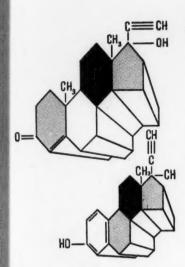
LABORATORIES, INC. KENILWORTH, N. J.



why is this woman tired?

Because she is mentally "done in". Many of your patients—particularly housewives—are crushed under a load of dull routine duties that leave them in a state of mental and emotional fatigue. For these patients, you may find 'Dexedrine' an ideal prescription. 'Dexedrine' will give them a feeling of energy and well-being, renewing their interest in life and living. Dexedrine* (dextro-amphetamine sulfate, S.K.F.) available as tablets, elixir, and Spansule* capsules (sustained release capsules, S.K.F.) and is manufactured by Smith Kline & French Laboratories, Philadelphia.
*T.M. Reg. U.S. Pat. Off.

July



to regulate the menstrual cycle

"do as the ovaries do"

Duosterone

anhydrohydroxyprogesterone 10.00 mg.

primed by ethinyl estradiol 0.01 mg.

per table

a physiologic regulator

For Simplified, Oral Treatment of Secondary Amenorrhea: infrequent periods, subnormal flow, Dysfunctional Uterine Bleeding: menorrhagia, relapse after curettage, irregular or too frequent periods, prolonged or profuse menses.

other indications

Habitual abortion, threatened abortion, functional sterility, dysmenorrhea, and premenstrual tension have responded to DUOSTERONE therapy.

action

DUOSTERONE simulates the normal ovarian endocrine pattern of the secretory phase of the menstrual cycle. A normal cycle may be set off by DUOSTERONE stimulation, much as touching the pendulum starts a wound clock. Normal menstrual function is safely and conveniently restored with essential, two-hormone action provided by DUOSTERONE: (1) Administration of needed progesterone, and (2) Estrogen priming, which is indispensable to adequate progesterone activity.

DUOSTERONE may also initiate an endocrine chain-reaction resulting in spontaneous ovulatory cycles according to the concept of Holmstrom.*

dosage

5 to 10 tablets per day for five days, beginning exactly one week before expected onset of menses. No medication is given on last two days. Repeat dosage for six successive cycles to ensure reestablishment of normal function.

supplied

Bottles of 25 and 100 tablets. On prescription only.

*Am. J. Obst. & Gynec., 68:1321, 1954.

ROUSSEL

ROUSSEL CORPORATION • 155 East 44th St., New York 17, N.Y.

Small diameter, ESTRONE PELLETS, ROUSSEL, 50 mg., for subcutaneous injection of pure, crystalline estrone to relieve menopausal symptoms for 3 months, according to the technique of TeLinde. (Johns Hopkins Hospital.) Write for literature. (1.) TeLinde, R. W., Operative Gynecology, 2nd Ed., J. B. Lippincott Co., Philadelphia, 1953.

dull emo

rine eling

and

nith

ynec

because anemia complicates so many clinical conditions . . .





'Trinsicon'

(HEMATINIC CONCENTRATE WITH INTRINSIC FACTOR, LILLY

serves a vital function in your total therapy

Potent 'Trinsicon' offers your patient complete and convenient oral anemia therapy; provides therapeutic quantities of all known hematinic factors. Just 2 Pulvules 'Trinsicon' daily produce a standard response in the average uncomplicated case of pernicious anemia (and related megaloblastic anemias) and provide at least an average dose of iron for hypochromic anemias, including nutritional deficiency types. In bottles of 60 and 500, at pharmacies everywhere.

POTENT • CONVENIENT • ECONOMICAL

TH ANNIVERSARY 1876 . 1956 / ELI LILLY AND COMPANY

American Journal of Obstetrics and Gynecology

Vol. 72

JULY, 1956

No. 1

Original Communications

THE USE OF UNLIMITED NONSTERILE VAGINAL EXAMINATIONS IN THE CONDUCT OF LABOR*

Frank J. Fara, M.D., Marsh Steward, Jr., M.D., and John Standard, M.D., Chicago, Ill.

(From the Department of Obstetrics, Cook County Hospital, and the Department of Obstetrics and Gynecology, University of Illinois College of Medicine)

IN 1847 Semmelweis began an investigation of the frightful incidence of puerperal infection and subsequent mortality accompanying delivery in patients of the Vienna Lying-In Hospital. He concluded that puerperal infection was essentially a wound infection resulting from the introduction of septic material into the birth canal by the examining hand of the obstetrical attendant. Four years prior to the writing of Semmelweis, Oliver Wendell Holmes clearly proved that the epidemic forms of puerperal sepsis, at least, were the result of improper precautions on the part of the physician during the conduct of labor. In 1894, Reis and Kronig independently introduced the rectal examination in an attempt to eliminate part of this contamination.² Present-day American obstetrics teaches that "... the birth canal be regarded as forbidden territory whose invasion by finger or instrument should be undertaken only on strict indication. Every introduction of the finger into the vagina during labor is attended by some risk of conveying infection. Insofar as is possible, therefore, labor should be conducted by abdominal and rectal examination only...."

While agreeing with the basic tenets set forth above and particularly with the basic concept of cross-infection among patients, we believe that the mere entering of the birth canal with a clean gloved hand has been unnecessarily condemned. As a result there has developed an unwarranted hesitation on

^{*}Presented at a meeting of the Chicago Gynecological Society, Jan. 21, 1955.

Note: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

the part of the obstetrician to make use of a swift and accurate method of obstetrical evaluation. This study consists of a review of the literature and the presentation of a series of 735 patients whose labors have been followed by nonsterile vaginal examination. It is the result of our desire to separate fact from fiction regarding the procedure and to determine the real danger involved, if any.

In the last thirty years only six articles have appeared on this subject, two American and four Russian. The first American report, that of Ralph A. Ries,³ was published in 1924. He presented a series of 609 patients examined vaginally during labor and concluded that vaginal examination did not differ materially from rectal examination in so far as the incidence of puerperal morbidity was concerned. He employed sterile water, however, and evidently limited the number of examinations to one or two. From 1949 to 1952 four articles were published in Russia purporting to show that no danger attends the use of vaginal examination in labor.4-7 The four Russian articles are mentioned merely for the sake of completeness as their bulk is devoted to an apparent controversy as to whether women in labor should be examined or merely observed. In addition their method of examination and statistical presentation is obscure. The most recent report, that of Prystowsky, appeared in August of last year. Reporting on 364 patients examined vaginally, he concluded that multiple vaginal examinations could be used with relative impunity. While he did several examinations and examined patients in bed, his series differs from ours in that he cleansed the perineum with sterile water and used sterile gloves, a modification of the sterile vaginal technique.

Material and Methods

Our investigation was conducted at the Cook County Hospital in Chicago from September, 1953, through June, 1954. The Obstetrical Service at Cook County Hospital consists of three divisions: normal, surgical, and septic. Admissions to all three divisions rotate serially through the services of six attending staff members. The patients selected for study in this investigation were all those admitted to the normal obstetric division on the service of one attending man (Dr. Fara) during the period mentioned. This yielded an unselected group of patients in normal or near-normal labor. Any patient with

an antepartum infection was excluded.

All patients received the routine soap-and-water perineal preparation and were shaved. When there was sufficient time, patients were given an enema. The vaginal examinations were conducted with no further cleansing except in an occasional case of gross fecal contamination of the perineum. When this occurred, the perineum was wiped off with tap water sponge. Vaginal examinations were done in bed by members of the attending staff, residents, and interns. The gloves used were the same as used for rectal examination, i.e., old gloves which had been washed and autoclaved but with no attempt to keep them sterile. The number of examinations was not limited in any way, and as Cook County is a teaching institution, some patients were examined many times.

Patients were kept in the hospital for a minimum of five days post partum. Temperatures were taken and recorded four to six times a day. No patient received an antibiotic unless an elevated temperature persisted for several days or unless there were other urgent indications for its use. The patient was then discharged to our postpartum clinic where an examination at six weeks was conducted personally by one of the authors,

1

ζ

e

f

n

d

p

S

y

X

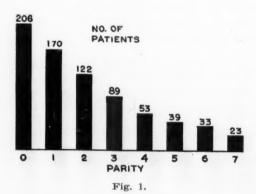
A simultaneous rectal control group was not run because of the difficulty involved in keeping that many additional patients in the hospital for the necessary period. Usually it is necessary to discharge patients after 48 to 72 hours in order to avoid overcrowding. Rather, a consecutive series of 800 patients delivered in a large university hospital in this city during the same time the vaginal series was under way was analyzed. In this latter hospital all labors are conducted by rectal examination except for an occasional sterile vaginal examination. Patients are kept an average of four to five days and temperatures are taken and recorded four times a day. Patients entering this hospital with antepartum temperature elevation were omitted from our study.

The definition of the term morbid is an elevation of temperature to 100.4° F. or above on any two consecutive days of the postpartum period excluding the first twenty-four hours. In addition, we determined the number of patients who had an elevation to 100° F. or over at any time during their hospital stay except the day of delivery. We feel that this latter determination is a more sensitive indicator of the development of a morbid process. Our statistical studies are primarly based on the latter figure. We believe that in this series an elevated temperature can be relied upon to give a reasonably accurate index of infection in view of the fact that antibiotics were not used unless urgently indicated.

There were 735 patients studied. The age distribution of the series varied from 14 to 44 years, with the majority between 16 and 30 as might be expected.

There were 206 nulliparas and 529 multiparas, with a range of 0 to 7 or more deliveries. The exact parity figures are presented in Fig. 1.

GRAPHIC PRESENTATION OF THE PARITY SPREAD OF THE SERIES



Of the 735 patients in the vaginal group 2.5 per cent were morbid by definition. This is higher than the 1.1 per cent found in the 800 consecutive deliveries followed by rectal examination. This difference approaches but does not reach statistical significance. Also, when one determines the total number of patients who had a temperature elevation to 100° F. or above on any day except the day of delivery, the two groups are identical: 12.9 and 12.8 per cent.

Antibiotics were administered to 15.3 per cent of the 800 rectal patients but to only 3.6 per cent of the 735 vaginal patients. We believe that the difference in formal or defined morbidity is due to the increased administration of antibiotics in the rectal group and not to a difference in the method of examination. This view is supported by the identical incidence in the two groups of patients showing an elevation of temperature to 100° F. or above. This

latter figure might be termed beginning morbidity. In the vaginal group formal morbidity was allowed to develop. In the rectal group it was frequently prevented from doing so by the administration of antibiotics.

In an attempt to learn as much as possible regarding the factors contributing to the production of temperature elevation, we have studied the vaginal group from several aspects. The first factor analyzed was the effect of length of labor. For this analysis, the series was arbitrarily divided into two groups: patients who had a labor of less than ten hours and patients who had a labor of more than ten hours. Analysis showed that in our series the length of labor had no significant effect on the production of morbidity (Table I).

Table I. Comparison of the Effect of Length of Labor on the Production of Postpartum Temperature Elevation

		1-10 Hours	0	VER 10 H	OURS
Total number of patients	489		246		
Total number of patients morbid and percentage	9	${(1.9\%) \choose (9.8\%)}$ 11.7%	10	(4.1%) (11.4%)	15.5%
Total number of patients febrile and percentage	48	(9.8%)	28	(11.4%))
			Chi squa Probabil		1.948

The second factor analyzed was the effect of premature rupture of the membranes on the production of a febrile course. The only two groups large enough for statistical analysis were at either extreme, one hour or less and ten hours or more (Fig. 2). No significant difference was found. The 12.0 per cent in the group of one hour or less and the 15.6 per cent in the group of ten hours or more render a probability of 0.4 of this occurring by chance, which is not statistically significant (Table II).

TABLE II. COMPARISON OF THE EFFECT OF ELAPSED TIME BETWEEN RUPTURE OF MEMBRANES AND DELIVERY ON POSTPARTUM TEMPERATURE ELEVATION

	1	HOUR OR LESS	10	HOURS	OR	MORE
Total number of patients	359		122			
Total number of patients morbid and percentage	8	$(2.2\%) \ (9.8\%)$ $\} 12.0\%$	4	(3.3% (12.3%)]	- 15.6%
Total number of patients febrile and percentage	35	(9.8%)	15	(12.39	6))	
			Chi squ	are		.869
			. Probabi	ility		.4

Third, in comparing the effect of one vaginal examination with that of many vaginal examinations as to the probability of producing a febrile post-partum course, we again found no significant difference (Table III, A). When the series was divided into two groups, one with three or less examinations and the other with four or more, we still failed to show a difference. On the basis of our analysis, the number of examinations undergone is irrelevant (Table III, B).

Parity, however, might appear to be significant. Twenty-one and fourtenths per cent of the nulliparous patients ran a postpartum fever as opposed to 9.6 per cent of the multiparous patients, a statistically significant difference (Table IV). This difference between the nulliparas and multiparas, however, p

e t o o e y

r-

ie

ge

.0 of e,

ES

of st-

en

ns

he

nt

ed

ce

er,

TABLE III. COMPARISON OF THE EFFECT EXERTED BY ONE OR MORE VAGINAL EXAMINATIONS ON POSTPARTUM TEMPERATURE ELEVATION

	a
£	Ł
	_

	1 EXAMINATION	MULTIPLE EXAM.
Total number of patients	129	606
Total number of patients morbid and percentage	$\left. egin{array}{c} 3 & (2.3\%) \ 10 & (7.8\%) \end{array} ight\} 10.1\%$	$\left\{ egin{array}{ccc} 16 & (2.6\%) \ 67 & (11.1\%) \end{array} ight\} 13.7\%$
Total number of patients febrile and percentage	10 (7.8%)	67 (11.1%)
		Chi square 1.321 Probability .25
	B	
4	1-3 EXAMINATIONS	4-10 EXAM. OR MORE
Total number of patients	382	353
Total number of patients morbid and percentage	$\left.rac{7\ (1.8\%)}{35\ (9.2\%)} ight\}11.0\%$	$\left\{ \begin{array}{c} 12 \ (3.4\%) \\ 41 \ (11.6\%) \end{array} \right\} 15.0\%$
Total number of patients febrile and percentage	35 (9.2%)	41 (11.6%)
		Chi square 2.313 Probability .15

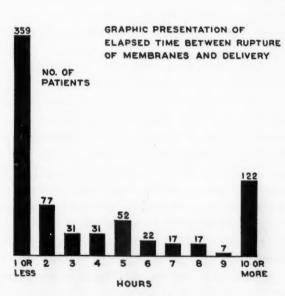


Fig. 2.

is due only to the increased incidence of episiotomy in the former (Table V) and not to the length of labor, increased number of examinations, or to a complicated operative delivery.

Investigations of the type of delivery undergone by the patient and her subsequent febrile or afebrile course disclosed an interesting point. As might be expected, there is a significant difference between the group who had completely normal, spontaneous deliveries and the group with episiotomy-operative deliveries. As might not be anticipated, however, from our data the difference lies between doing an episiotomy and not doing an episiotomy. Once

an episiotomy was done in this series, it made little difference what additional procedure was carried out. The difference evidenced between the episiotomy and episiotomy-operative groups is not significant.

TABLE IV. COMPARISON OF THE EFFECT OF PARITY ON POSTPARTUM TEMPERATURE ELEVATION

		NULLIPARAS	MULT	IPARAS
Total number of patients	206		529	
Total number of patients morbid and percentage	9	$\left\{ \frac{(4.4\%)}{(17.0\%)} \right\} 21.4\%$	10 (1.99	$\left. egin{array}{c} \% \ \% \ \end{pmatrix} 9.6\%$
Total number of patients febrile and percentage	35	(17.0%)	41 (7.79	%))
			Chi square Probability	17.194

Table V. Comparison Between Normal Spontaneous Delivery, Episiotomy Only, and Operative Delivery on the Production of Postpartum Temperature Elevation (Operative Delivery Includes All Forceps, All Intrauterine Conversions of Position, and All Uterine Explorations)

	NORMAL SPONTANEOUS DELIVERY	EPISIOTOMY ONLY	OPERATIVE DELIVERY		
	A	В	C		
Total number of patients	460	153	122		
Total number of patients morbid and percentage	$\left. \begin{array}{c} 5 & (1.1\%) \\ 37 & (8.0\%) \end{array} \right\} 9.1\%$	${7 \ (4.6\%) \atop 21 \ (13.7\%)} $ ${18.3\%}$	$\left\{\begin{array}{cc} 7 & (5.7\%) \\ 18 & (14.8\%) \end{array}\right\} 20.5\%$		
Total number of patients febrile and percentage	37 (8.0%)	21 (13.7%)	18 (14.8%)		
		A/B	Chi square 12.342 Probability 0		
		B/C	Chi square .216 Probability .6070		

Summary

The literature for a period of thirty years on the subject of vaginal examinations during labor is reviewed. A series of 735 patients whose labors were followed by multiple nonsterile vaginal examinations is presented. The relationship of length of labor, type of delivery, parity, and ruptured membranes to the production of postpartum temperature elevation is analyzed. Patients formally morbid and total patients febrile are compared with a like group of 800 patients followed by rectal examination. This comparison showed a difference in defined morbidity in favor of the rectal group which approached but did not reach statistical significance. The total percentage febrile at any time in each group was found to be identical. The difference in formal morbidity is thought to be explained by the difference in the administration of antibiotics which was five times as great in the rectal group. We feel that this administration of antibiotics prevented those febrile and potentially morbid patients in the rectal group from becoming actually morbid. The only factor significantly affecting the production of temperature elevation in the analysis of the vaginal group was found to be episiotomy.

Conclusions

We have presented an obstetrical procedure dating back to antiquity, the precursor and basis of present-day obstetrical examination during labor. From the evidence gathered in this study, we feel that nonsterile vaginal

D

X-

rs

ne

n-

d.

re.

ed

ed ny

r-

of

is

id or sis

he

or.

al

examinations can be utilized to follow the progress of labor without risk to the patient and with markedly increased comfort to her. It is also obvious that a more accurate determination of the progress of labor which, incidentally, decreases the number of examinations necessary is possible by the routine use of vaginal examination.

Yet today this procedure has fallen into considerable disrepute and is condemned by authors and most of the leaders in our field. In the main, this condemnation is based on the statistical conclusions of Semmelweis, Holmes, and others of the days before aseptic technique became commonplace. The fear of sepsis is foremost in the minds of obstetricians and the feeling that the introduction of an unsterile examining finger into the vagina may promote sepsis has deterred many from this procedure, even though its advantages over rectal examination are well known.

A clean glove is far different from the contaminated finger of the obstetricians of Semmelweis' day, who went from septic to clean cases in a matter of steps with a complete absence of aseptic technique. Perhaps another deterrent to this procedure has occurred to many as it did to us, namely, that with its acceptance a few untrained individuals would perform this in the same way as Semmelweis and his students. But how many of the large percentage of patients not delivered in teaching or recognized institutions are having vaginal examinations during labor? We would venture to say that the figure would be high.

The paucity of obstetrical literature on this subject of rectal versus vaginal examination during labor prompted us to investigate the apparent harm thought to be inherent in this procedure. We found this apparent harm to be more nebulous than real. Since our series numbers 735 cases, we have presented this as a preliminary study and have demonstrated that nonsterile vaginal examinations during labor do not increase morbidity, but the final statement of their safety rests not on our series, but on a continuation of the investigation in several hospitals and areas.

We wish to express our gratitude to Dr. George H. Gardner and Wesley Memorial Hospital, Chicago, Illinois, for permission to review their records for the series of rectally examined patients.

References

- Eastman, N. J.: Williams Obstetrics, ed. 10, New York, 1950, Appleton-Century-Crofts,
- 2. Prystowsky, H.: Am. J. Obst. & Gynec. 68: 639, 1954.
- AM. J. OBST. & GYNEC. 8: 475, 1924.
- 4. Petrov-Maslakow, M. A.: Akush. gin Meskva. 4: 45, 1951.

- 5. Teverovskii, M. J.: Akush. gin Meskva. 4: 49, 1951. 6. Beloshappe, P. A.: Akush. gin Meskva. 3: 27, 1952. 7. Lipmanovich, S. G.: Akush. gin Meskva. 1: 27, 1949.

Discussion

DR. FREDERICK H. FALLS.—This paper is important because it upsets some of the ideas that we have accepted over the years which were transmitted to us by teachers who we felt knew whereof they spoke. I have never been quite sold on the dangers of sterile vaginal examination, and I have taught for a good many years that there is a disease which is detrimental to obstetricians as well as to patients, called vaginophobia. Vaginophobia is particularly dangerous to those patients who should have vaginal examinations and do not, to determine various complications. They do not have vaginal examinations because their doctors have been taught it is very dangerous to do vaginal examinations, even with sterile technique.

I believe this paper refutes pretty completely that point of view. The 700-odd cases is a group large enough to be statistically significant. There is no special safeguard in such cases that would not be provided in the cases in any ordinary well-conducted obstetrical department. With the conditions which we have at County Hospital, with 10,000 to 12,000 cases a year, the facilities of the wards are taxed to the utmost simply to get the patient in, get her scrubbed up and shaved, and the routine examinations made. If anything, they are cases in which, under the circumstances, one would expect more infections to occur. To offset this, it should be remembered that these patients were all delivered in the obstetrical operative suite, and that obstetrical suite is isolated from the rest of the hospital, and no indiscriminate visiting occurs; that these patients are all examined by residents and interns who are thinking and doing nothing but obstetrics. It is an entirely different problem than would occur if these patients were examined in this way by men who were doing general practice and in hospitals where the isolation facilities were not as good as they are at County Hospital. Therefore, I think this piece of clinical research, good though it may be as far as it goes in showing us that you do not necessarily contaminate the patient seriously by doing this type of examination, ought not to go out as having the stamp of approval of the Chicago Gynecological Society that sterile vaginal examinations are less dangerous than rectal examinations or that nonsterile vaginal examinations are just as safe as sterile vaginal examinations. I think it would be a mistake to permit that impression to be spread to the public and to the general practitioners and to the students and nurses who are conducting obstetrical cases. It would lead to lowering of the standards and to carelessness which might result fatally in a good many cases. We must remember, as we sit in on the Maternal Welfare Committee of the Illinois State Medical Society and study the maternal deaths, that about a third of the deaths are still due to puerperal infections.

All these patients, Dr. Fara has said, were not re-examined. It would have been more impressive if more than 252 out of the 735 had been re-examined. Maybe the serious complications all occurred among the other 483 cases. Of course, we know this would be very difficult at County Hospital. I can think of an additional study, which Dr. Fara indicated he is planning to do, that it might be better if every other patient were examined in the routine way, and every other one were examined by nonsterile technique as indicated. Another series could be run with every other patient examined rectally, and the alternate patients examined with nonsterile gloves. In other words, when we compare the results in two institutions we haven't as good a control as if all of the patients had been under the supervision of the same group.

I think this sort of work is valuable because it tells us what we do not know; it tells us what we have not had the intestinal fortitude to find out for ourselves. I have always taught that the rectal findings were not definite if a decision depending on those findings had to be made, and that it was mandatory that vaginal examination be made in order to get the best information possible. I am glad Dr. Fara has done this work, and I hope he will continue it in the spirit in which he has undertaken it. I suggest these minor changes in method in order that we may have some way of comparing these two techniques.

DR. BEN M. PECKHAM.—I had the privilege of observing how the control data in this study were gathered and analyzed against the data from County Hospital. The reason for this is that the control data came from Chicago Wesley Memorial Hospital. I also had the opportunity of reviewing the statistical methods used in their analysis. I think that this series of 700 patients is entirely adequate in size to demonstrate that under the conditions of the experiment there was no significant difference between the incidence of postpartum fever in the vaginal series and that in the control group. Further, the only significant factor among those analyzed by the author was episiotomy. I would like, however, to

n

0

f

.

e

ķ

S

2

1-

3.

0

e

a c-

d

d

10

10

n

18

e e

ra

re

as

ad

m-

ts

it

VA

Se

in

I

or

es.

in on

ad

his

ns

ım

nt

to

emphasize that the conditions of this experiment certainly do not correspond to the conditions found in most maternity hospitals. Here the vaginal examinations were done with few exceptions by people who were scrubbing regularly several times a day and on prepared patients using gloves which to all intents and purposes were sterile. In most maternities those doing the examinations have not recently scrubbed, often have just seen patients with pyogenic or other virulent bacterial infections, and are much more likely to contaminate badly a single sterile glove when putting it on.

I think these data further support the opinion that occasional vaginal examination in bed during labor for purposes of more accurate diagnosis is a harmless procedure when done under clean conditions.

DR. WALTER F. DILLON.—Because of the high incidence of puerperal sepsis, Semmelweis, Holmes, and DeLee laid great stress on antisepsis, and vaginal examinations were forbidden. Many of these were neglected cases of dystocia brought into the hospital already infected, however. Today nearly all patients are delivered in hospitals, and, because of a better evaluation of the pelvis early in labor, many of these dystocia cases are avoided, and hence there is less infection. In addition, we have the use of antibiotics. These, however, should not replace good obstetrical judgment, nor have us discard the lessons of the past.

Today the pendulum is in the center between two extremes, and the paper this evening has shown that vaginal examinations can be safely done in labor. My own preference is to use a sterile glove in the labor room, and to do a vaginal examination in all cases where there is any doubt regarding position, dilatation, bag of waters, or the cause of no progress. It tells the answer when rectal examination fails to do so.

DR. MARTHA SOLLNER.—I wish to state that at the former Wertheim Clinic in Vienna, where I was a resident from 1926 to 1932, at the time Prof. Kermauner was the head, we had no rubber gloves for the students. From October 1 to July 15, patients during delivery were examined by two or three students with good clean hands but without gloves, and no infections occurred. The patients were not accustomed to being examined any other way. The clinic had 2,500 to 3,000 obstetrical patients a year. From July 15 to October 1 there were no students present, and at that time we used sterile gloves for vaginal examination. Before I came to Chicago, neither at the Clinic nor later on in my office, did I examine patients during delivery rectally except a very few times.

In Vienna most of the patients were examined for the first time when they entered the hospital for delivery. They stayed about eight to ten days after delivery. There were many more primiparas in Middle Europe than in Chicago. I cannot remember the exact figures, but about half of the patients were married, and about 70 per cent were primiparas and about 30 per cent were multiparas. No infections occurred when the primiparas were examined vaginally on the tenth day after delivery. We examined the lower part of the vagina. The multiparas were examined on the eighth or ninth day before being disharged without the occurrence of infections. In case there were classes for American doctors, every examiner had sterilized gloves. The doctors were trained to have clean hands. The students who came during the winter term mostly lived at the hospital for a week or eight days, during the summer term for five days. They were told to take care of their hands for ten days or two weeks before their training at the hospital. Neither for students nor for teacher were gloves available, and no infections occurred.

DR. EDWIN J. DECOSTA.—Thirty years ago Dr. Ralph Reis nicely demonstrated that vaginal examination under proper or so-called sterile technique did not contribute to maternal morbidity. Even repeated examinations could be performed almost with impunity. I have a feeling that what we have listened to tonight is a report of a technique in no way different from that of thirty years ago except that we have eliminated the draping, the cleansing and other trimmings usually associated with vaginal examinations during labor.

The gloves the essayists used were probably sterile. I would like to ask Dr. Fara if they ever checked the gloves by culture for the presence of microorganisms.

DR. JOHN R. WOLFF.—The Armed Forces of our country award medals for extraordinary services. I do not think that either the authors or some of the discussants would receive the good conduct citation. However, they might be given the Medal of Honor. This award is given for bravery in the face of enemy action above and beyond the call of duty.

DR. CHARLES E. GALLOWAY.—I wish to support Dr. Falls' remarks because I do not believe that this Society should permit a paper of this type to be presented for publication, and I doubt very much if it should have been presented even under the circumstances tonight. I think the next thing to occur would be that someone would come before us and say that you should not even shave the patients, that you should let them alone and just wash them up.

I do not believe this Society can permit publication or give its sanction for publication of a paper based on no more patients than this, and especially patients at Cook County Hospital. I do not believe Cook County Hospital is any place to start any innovations in obstetrics because it does not represent a cross section of our population, and if this paper is published and goes out over the country and young fellows read it, as has been said here tonight, practically only by its title, there is going to be harm done.

I do not know very much about statistics, but to me 19 is twice 9 at least, and you had a figure of 19 for the morbidity on your vaginal examinations as compared with a figure of 9 on rectal examination. That part of the paper I did not fully understand. To me it is of some significance, and I believe considerable work should be done on this problem before we approve it for publication in some national medical magazine which would be read by a considerable number of the medical profession.

I believe this Society should be more careful about its reputation than to turn this thing loose.

DR. H. CLOSE HESSELTINE.—It is general knowledge that patients who have prolonged labors and those with more than the usual manipulation are more likely to develop a febrile reaction, in the puerperium if not during labor. This seems directly related to the fact that bacteria begin their invasion of the uterus in early labor. Undoubtedly rectal as well as vaginal examinations contribute to more rapid bacterial invasion of the uterine cavity. Even so, vaginal examinations properly done have a real place in modern obstetrics. Any study which increases our knowledge or comprehension is commendable, provided it is within the recognized framework of medical research. This study, however, appears without sufficient control factors.

Every investigator must carry the responsibility of the influence of his study, and should be able to show justification for the study and the methods used.

When one speaks of the number necessary for such a study, a larger number is necessary because in good maternity service today there is an incidence of only 5 to 8 per cent febrile puerperal patients.

Ungloved hands have been used with reasonable safety, but the risks and potential danger of this practice cannot be justified on a basis of economy. What may be normal bacteria for one individual may not be normal for another. Sterile vaginal examinations are good teaching procedure but who can point to a single reason for contaminated glove examination.

A heavy responsibility falls upon the authors in their advocacy of contaminated gloves in vaginal examinations. "Unlimited examinations" is a very wide term. Perhaps it would have been more appropriate to call it Management of Labor by Contaminated Gloved Hands.

The authors adhere to one point of asepsis. They did not have sufficient confidence of protection to themselves without the use of gloves. This point alone casts doubt upon the entire project and the conclusions.

DR. FARA (Closing) .- I am afraid that time will not permit rebuttal of everything that has been said. It has been very flattering for the most part. We hoped the paper would cause much discussion, and I think it has.

I hope we have refreshed your memories of the big production put on every time you want to do a sterile vaginal examination. It requires at least ten sheets and then you are permitted to do a sterile examination. We believe that in doing it in the manner we have described, we can obviate taking the patient to the delivery room, going through the usual cumbersome routine, etc.

I am very happy that Dr. Fitzgerald was more or less in accord with me. Since he saw my data, I expected he would be. He took exception to a few things, however. First, the apparent innocuousness of long-ruptured membranes and the length of labor-in these patients we found them not as important as we have been taught. (Perhaps a shibboleth?) I think it would be well to stress that as far as sepsis is concerned, we have proved that when episiotomy is done the incidence of febrile reaction is increased. With operative delivery or intrauterine manipulation the incidence of morbidity is so little increased after episiotomy that it is statististically insignificant.

As to the series being too small, we deny that it is; 735 patients are a good-sized series. The reason we did not have a larger series is that our Board of Health does not permit overcrowding. We delivered something over 12,000 patients last year and we could not keep all of them five days.

Referring to Dr. Falls' remarks, I realize that we upset ideas which we all have (vaginophobias), and we tried to. In my capacity as a private hospital consultant, I find so often that things would have been easier if the patients in labor were permitted to have vaginal examinations indiscriminately. I know that the rules of the Board of Health in many places say that sterile vaginal examinations may be done only under certain indications and restrictions.

As far as cross-infections are concerned, this has been outdated. We know that all recognized hospitals keep patients with infections separate from the normal or near-normal, so we are not dealing with cross-infection.

Dr. Falls also questioned why we didn't have a rectal group control series. Again, it was only because we can keep a few patients for five days. We have to get them out of the hospital because of space limitations.

I appreciate Dr. Peckham's remarks about 735 being a good-sized number of cases in that these were statistically analyzed. This may sound like a small number, but the statistical significance would be the same whether we had 735 or 735,000, and the probabilities would still be the same.

He questions the preparation of the patients. These were patients who were washed and shaved, as is done in every hospital. As far as putting on gloves is concerned, we picked them off the pile and pulled each finger on with the other bare hand, and then they were no longer sterile. They were sterilized but no further attempt was made to keep them sterile.

Dr. Sollner said that in Vienna and in Europe in general, vaginal examinations are done routinely and rectal examinations are almost unheard of. She has said that their morbidity rate is no higher than ours.

Dr. Hesseltine mentioned the question of microbiology and what he said is, of course, perfeetly true. However, we now have fewer infections in obstetrical patients. I recall that, a relatively short time ago while I was a resident, we always had patients on Ward 41 dying of sepsis, four, five or six of them on any day. Now if we have a patient dying of sepsis it is a rare thing. Even in episiotomies we used silkworm-gut and figure-of-eight sutures to permit removal for drainage if they became infected as they often did. We do not see this type of infected episiotomy today and we sew them up tightly. We do not have suppurative mastitis as we did in the past.

IS THE STANDARD OF OBSTETRIC MORBIDITY SERVING A USEFUL PURPOSE?*

IRVING SIEGEL, M.D., CHICAGO, ILL.

(From the Departments of Obstetrics and Gynecology of Mount Sinai Hospital and The Chicago Medical School)

THE purpose of this paper is to demonstrate that the answer to the above question is probably in the negative.

Obstetric morbidity has become increasingly rare as a subject for articles. It is hoped that this paper may help to relegate the standard of morbidity to its proper historical position.

The present standard of morbidity adopted by the American Joint Committee on Maternal Welfare is defined as follows:

"A temperature of 100.4° F. (38° C.) or higher occurring on any two of the first ten days postpartum exclusive of the first twenty-four hours constitutes febrile morbidity. The temperature is to be taken by mouth by a standard technique at least four times daily."

Regulations of the Department of Public Health of the State of Illinois require all maternity hospitals to submit monthly reports including the incidence of morbidity based on this standard, regardless of the individual institution's method of tabulation. The morbidity is reported under the heading of "infection."

The terms "puerperal morbidity," "obstetric morbidity," "febrile morbidity," and "postpartum infection" are often used interchangeably.

In this paper certain terms will have the following meanings:

Morbid or morbidity: according to the standard.

Febrile: elevation of temperature to 100.4° F. or higher on any day, excluding the first 24 hours post partum.

One-day fever: elevation of temperature to 100.4° F. or higher for one day only.

Afebrile: no elevation of temperature to 100.4° F., excluding the first 24 hours post partum.

The incidence of morbidity in puerperas is expressed in percentage of the total number of patients. This percentage is directly proportional to the maternal mortality due to infection.^{1, 2}

The incidence of febrile morbidity has from the time of inception of the standard been one criterion of the character of the obstetrics performed and the degree of asepsis employed.

The difficulties inherent in the application of any arbitrary standard of morbidity have often been pointed out.², ³, ⁴, ⁶, ⁷, ¹¹

t

^{*}Presented at a meeting of the Chicago Gynecological Society, May 20, 1955.

e

e

0

1-

of

n-

is

n-

n-

ng

r-

he

1a-

he

nd

of

Obvious factors which may influence the reportable incidence of morbidity include, but are not limited to:

- 1. The technique of taking the patient's temperature and the accuracy of the thermometer.⁵
- 2. The frequency of temperature determinations. Previous to 1941, the temperature was recorded at least four times daily. Currently, it is recorded twice daily, morning and afternoon, unless elevations above normal or patient's complaints suggest repeat determinations.
- 3. The length of hospitalization. The earlier the mother is discharged, the less chance for fever to develop during the hospital stay. Prior to 1943, the average stay was ten days; now it is five to six days.
- 4. The precision with which the standard of morbidity is applied to temperature readings.
- 5. The use of sulfonamides and antibiotics. From 1937 to 1943 the sulfonamides were available; from 1943 to date the antibiotics have been extensively used. The administration of antibiotics on the first febrile day may "knock out" any infection and render the patient afebrile; thus the case escapes the classification of morbidity under the standard.

The reduction of morbidity and maternal mortality due to infection in the last ten years has been ascribed to many factors. While the antibiotics seem to have received the lion's share of the credit, other elements in medical progress have been considered important. Rarely is improvement in one phase of medical care the result of a single factor. In an analysis of the effect of antibiotics on the obstetric morbidity, it should be emphasized that other principles in obstetrics have not remained static. For example, during the antibiotic decade (1942–1952) changes included but were not limited to: (a) increased availability and use of transfusions; (b) more hospital deliveries; (c) early ambulation; (d) widespread dissemination of medical facts in lay magazines; (e) better education of physicians in obstetrics; (f) better and greater application of prenatal care.

These factors have been stressed repeatedly in the literature.

One is also aware of the fact that mere concomitancy is not always indicative of an additive effect. The harmful effect of a new procedure may be canceled out by the simultaneous institution of another change. The degree of asepsis employed in 1952 was no greater and probably less than in 1942; this is evidenced by the gradual introduction in the last decade of more and more "daring" obstetric procedures, daring in the sense that they are diametrically opposite to the fundamentalist's concept of asepsis.

To implement the purpose of this paper, the morbidity statistics for the years 1942 and 1952 will be compared; the effect that antibiotics have had on the incidence of morbidity and one-day fevers will be demonstrated; and the present standard of morbidity will be realistically evaluated.

Procedure

The morbidity statistics for the years 1942 and 1952 of the Department of Obstetrics of Mount Sinai Hospital were reviewed. These two years were

selected because they are the limits of a decade in which antibiotic therapy developed, and the interval is convenient for statistical comparison.

The microfilms of the charts of all obstetric patients delivered in the hospital in the year 1942 were scrutinized. This was necessary in order not only to examine the records of morbid patients but also to detect the temperature graphs which showed one-day fevers.

The daily temperature books of the obstetric floor were examined for the year 1952. The hospital charts of all patients who had fever were pulled from the files of the medical record room.

The standard of morbidity was strictly applied to all febrile cases. Note was made whether or not the patient had received sulfonamides or antibiotics.

Data

The incidence of febrility in 1952 was less than one-half the incidence in 1942.

TABLE I. INCIDENCE

	1942	%	1952	%
Deliveries	1,439	100.0	2,002	100.0
Febrile cases	105	7.3	70	3.4
Morbid	49	3.4	31	1.5
One-day fever*	56	3.9	39	1.9

*On or before the sixth day post partum.

The reduction of the incidence of morbidity in the decade 1942-1952 parallels the decrease in morbidity in other Chicago hospitals and in the State of Illinois as a whole.¹⁰

The one-day fevers were compared on the basis of six days' hospital stay. This was the average in 1952; in 1942 the average stay was ten days.

Observe that the incidence of morbidity and of one-day fever was almost equal in each of the two years. The significance of this is not clear; it may mean that there is an equilibrium between one-day fevers and morbidity.

As the febrile cases were being tabulated, the high incidence of fever in cesarean sections became apparent (Table II).

TABLE II. INCIDENCE OF FEVER IN CASES OF CESAREAN SECTION

	1942	%	1952	%
Total febrile cases	105	100	70	100
Cases of fever in cesarean sections	19	18	33	47

These figures became more striking when the incidence of morbidity in cesarean section was compared (Table III).

TABLE III. INCIDENCE OF MORBIDITY IN CASES OF CESAREAN SECTION

	1942	%	1952	%
Total cases of morbidity	49	100	31	100
Cases of morbidity in cesarean section	14	28	20	64

TABLE IV. INCIDENCE OF CASES OF MORBIDITY IN CESAREAN SECTION IN RELATION TO ALL CASES OF SECTION

	1942	%	1952	%
Total No. cesarean sections*	47	100	92	100

*In 1942 the cesarean incidence was 3.3 per cent; in 1952 the incidence was 4.6 per cent.

n

n

nt.

The first impression one might obtain from these figures is that the incidence of morbidity in cesarean sections was much higher in 1952 than in 1942. That this deduction is spurious can be seen when only cesarean sections are compared (Table IV).

Statistically, the decrease of morbidity from 30 to 22 per cent is not significant. In 1953, however, 78 cesarean sections were done; the incidence of morbidity was 15 per cent. This decrease from the 30 per cent incidence in 1942 is significant. It may be said, therefore, that the reduction in morbidity in 1952 showed a definite trend.

Morbidity in 1952 seemed to be limited almost to the cesarean section patients. Since the cesarean section presents the optimal biologic conditions for infection, it was felt that antibiotics would receive their greatest test in these operative cases. Accordingly, a study was made of the frequency with which antibiotic drugs were administered to cesarean section patients.

TABLE V. FEVER IN CESAREAN SECTION PATIENTS WHO WERE GIVEN MEDICATION

		MIDES, 1942 CASES)		rics, 1952 (ASES)
	NO.	%	NO.	1 %
Afebrile	0	0	38	41.3
One-day fever	4	8.5	12	13.0
Morbid	12	25.5	20	21.7
Total	16	34.0	70	76.0

TABLE VI. FEVER IN CESAREAN SECTION PATIENTS WHO WERE GIVEN NO MEDICATION

	1942	%	1952	%
Afebrile	28	59.5	21	22.8
One-day fever	1	2.1	1	1.0
Morbid	2	4.2	0	0
Total	31	65.8	22	23.8

No antibiotics were available in 1942; it will be noted that sulfonamides were given charily and mainly to morbid patients. On the other hand, in 1952, antibiotics were administered lavishly (41 per cent to afebrile patients; 76 per cent of all cesarean section patients received antibiotics).

Comment

The familiar challenge that many of the patients received antibiotics needlessly and that the reduction of morbidity may be merely a "nonsense correlation" may be answered as follows:

It is true that one cannot determine accurately whether all 38 afebrile patients in 1952 were afebrile *because* of the antibiotics or *despite* the drugs. Similarly, one cannot say definitely that all the one-day fevers would have progressed to morbidity had not antibiotics been given.

The proof of the efficacy of antibiotics, prophylactically and therapeutically, however, need not be demonstrated in this paper. The value of antibiotics has been proved by many investigators, s, beyond the shadow of a doubt. For my purpose it suffices to show that the so-called indiscriminate use of antibiotics results in a remarkable reduction in the incidence of febrile reactions.

Subtract the cesarean section morbidity and the incidence of morbidity in 1952 would then be about 0.5 per cent. This may be considered almost the irreducible minimum.

On the other hand, in cesarean sections the reduction in morbidity was not spectacular though the trend was unequivocal.

It is realistic to assume that published reports of contraindications to, and unfavorable reactions from, antibiotics, and the "deplorable" manner in which antibiotics are used have apparently failed to halt the so-called indiscriminate use of the drugs. The net result seems to have been a continuing reduction of morbidity. As in other fields of medicine, antibiotics have caused havoc in attempts to maintain the status quo of some of the fundamental concepts of infection and its control.

The standard of morbidity may be considered today as unreliable and outmoded. It would be more practical and meaningful to report clinical infections under standard nomenclature. Under the onslaught of antibiotics, fever, per se, is rapidly losing its significance, statistically and otherwise.

Conclusions

- 1. Antibiotics have probably been the greatest contributory factor in the reduction of morbidity to the remarkably low incidence of approximately 1 per cent.
- 2. Most of the febrile reactions in obstetrics occur in cesarean section patients.
- 3. The present standard of morbidity is neither meaningful nor purposeful because: (a) Few, if any, institutions comply with the terms of the definition of morbidity. (b) In general, antibiotics "indiscriminately" administered have tended to confound the original purpose of the standard of morbidity, namely, to serve as an index of the character of the obstetrics practiced in the hospital and the degree of asepsis employed. (c) Arbitrary standards of fever have never been accepted as truly representative of clinical infection.
- 4. It is recommended that the present standard of morbidity be abandoned; instead, infections should be reported under clinical diagnostic terminology, regardless of the degree of febrility.

The assistance of Mr. John Gilbert, biostatistician, Department of Oncology, The Chicago Medical School, is gratefully acknowledged.

References

- Crofts, Inc., p. 929.

 2. Watson, B. P.: In Curtis, A. H., editor: Obstetrics and Gynecology, Philadelphia, 1933, W. B. Saunders Company, vol. 2, p. 218.

 3. Stander, H. J.: Textbook of Obstetrics, New York, 1945, Appleton-Century Co., Inc., p. 1165.

- 4. Stander, H. J.: Am. J. OBST. & GYNEC. 28: 421, 1934.
 5. Dimond, E. G., and Andrews, M. H.: J. A. M. A. 156: 125, 1954.
 6. Welton, T., Glass, M., and Mazzola, V. P.: Am. J. OBST. & GYNEC. 21: 263, 1931.
 7. DeLee, J. B.: The Principles and Practice of Obstetrics, ed. 5, Philadelphia, 1930, W. B. Saunders Company, p. 930.

8. Harris, L. M., and Shook, D. M.: Am. J. Obst. & Gynec. 57: 1186, 1949. 9. Keettel, W. C., Scott, J. W., and Plass, E. D.: Am. J. Obst. & Gynec. 58: 335, 1949. 10. Selected Statistics in Hospital Maternity Service, Illinois Dept. of Public Health, 1943 and 1952.

11. D'Esopo, D. A.: Am. J. OBST. & GYNEC. 59: 77, 1950.

2750 W. 15TH PLACE CHICAGO 8, ILLINOIS

Discussion

DR. H. CLOSE HESSELTINE.—If a standard does not or has not served a purpose, then it should be discarded. If, however, modification is justified, it should be changed, but when it is adequate in the present form, it may well remain unchanged. Today the standard originally devised by the American Committee on Maternal Welfare is not serving the same useful purpose. Nevertheless, standards for febrile or other morbidities should not be discarded because improvement has occurred; rather let us bring the standard up to date. It has been well established by physiologists that man has a "normal" temperature range. The upper limits of normal were placed at 99.9° F. or 37.7° C.

With this in mind, Bustamante and Hesseltine modified the proposal of D'Esopo. His proposal was to use the tenths of the degrees elevations above 99° F. (Our modification was to take the accepted normal of 99.9°.) He totaled the tenths of degree above and then removed the decimal point, thus leaving a whole number. This represented the total febrility or febrile index. We took the 37.7 or 99.9 as the arbitrary dividing point between temperatures and fever. Since most thermometers (Fahrenheit or Centigrade) are calibrated in fifths of a degree, there will be a sharp separation. We added tenths of degrees and eliminated the decimal point in the same fashion. This represented the febrile index. In order to indicate the febrile days involved, the number is given by a hyphen after the index figure. This experience can be transmitted readily and promptly by either visual or auditory media. It could also be depicted in graph form. In the graph the height represents the total number of tenths of degrees' elevation, whereas the horizontal represents the number of days.

It is abvious that the newer drugs have contributed to the improvement. Even so, part of the improvement must be credited to better medical care, correct use of blood, proper electrolytes, and a number of other agents. Bustamante, Loth, and Hesseltine investigated the influence of antibiotics upon the intrauterine puerperal flora. It was not possible to make any real progress toward the elimination of bacteria from the puerperal uterine cavity, but the percentage frequencies varied greatly and unfavorably at times. Some patients became febrile while on antibiotics, no doubt because the bacterial balance was altered which allowed certain strains to thrive at the patient's expense.

The puerperal uterine cavity is in some ways similar to a chronic abscess cavity. The obstetric patient is not an aseptic patient. She is no worse than she was twenty years ago. As a matter of fact, she is even safer. But, by comparison today, the average gynecologic surgical patient is cleaner and safer. The time may come when the gynecologic patients may need to be protected from the obstetric patient rather than the situation which has existed and which should be changed.

I take frank exception to the statement that the "so-called indiscriminate use of antibiotics" caused a remarkable reduction in the incidence of febrile reaction. It is not the indiscriminate use but the intelligent employment that has paid off. It is an established fact that a number of organisms may develop resistances to antibiotics, and thus the value of antibiotics can be lost. There is also the risk of sensitization. Accordingly, antibiotics should be used properly and consistently, based upon sound medical practice; that is, used in sufficient amounts for sufficient length of time and on real indications.

Cesarean section receives undue blame too often. It is not cesarean section but the indications and contraindications that should be evaluated. The incidence will not be identical in all hospitals for the nature and type of patients, the amount of complication, and the number of referrals of special cases are factors that must alter the individual incidence somewhat.

In summary, Dr. Siegel says again that the indiscriminate use of antibiotics tended to confound the original purpose of the standard of morbidity. Does Dr. Siegel mean indiscriminate use of antibiotics?

He has used the word "morbidity" specifically for the febrile course. Any patient who is ill, whether it is toxemia, infection, anemia, or any other complication, is morbid in one sense—she is ill or abnormal. Would it not be more correct to have morbidity standards for some of the more common complications? Perhaps something could be worked out for the other complications paralleling the proposal of D'Esopo or with modifications by Bustamante and Hesseltine. I believe in standards—are we good enough to throw away standards? If not, then we should bring the standards up to date. The condemnation of practice is a negative action. A constructive suggestion to sharpen our attention would be in order.

I commend Dr. Siegel for approaching a controversial subject, because there will be those who are reluctant to make a change because they are opposed to a change. Certainly we should not be the last to give up the old, nor should we be the first to give up that which has been proved to be good. We should be open minded and progressive by evolution. We should not be rebels for the sake of rebellion, but are entitled to lead in the agitation for constructive purposes.

CESAREAN SECTION IN MULTIPLE PREGNANCIES

SIMON BRODY, M.D., BROOKLYN, N. Y.

(From the Department of Obstetrics and Gynecology of the Unity Hospital)

THE subject of cesarean section is very prominent in modern obstetrical literature. The indications, contraindications, incidence, comparative incidence, increasing incidence, greater safety, abuse, and danger of the operation, as well as pleas for restraint and caution, are being constantly discussed. In this voluminous material, very little reference could be found regarding the relationship of cesarean section to multiple pregnancy.

The reason for the paucity of information on this subject is, probably, due to the fact that multiple pregnancy per se does not constitute an indication for cesarean section.

Lull, in a series of 789 cases of cesarean section, listed three cases in which the indication for operation was multiple pregnancy. He does not state how many cases of twins were delivered by cesarean section in the entire series.

Similarly, Zettelman and Bowers² listed one case in which the presence of twins was the indication for section in a series of 896 cesarean sections. Irving³ stated that, in 1,887 sections, there were 24 sets of twins. He further stated that more than half of these cases were probably not recognized as twins before the section was performed.

Within the last few years several twin pregnancies were encountered which posed special problems. These patients were delivered by cesarean section, some because of, and others regardless of, the presence of multiple pregnancy. It became interesting to ascertain whether the indications for cesarean section, as well as its incidence in multiple pregnancies, differed in any way from the indications for, and the incidence of, this operation in single pregnancies.

With this thought in mind, a review was made of all the deliveries at two hospitals during a five-year period, from Jan. 1, 1950, to Dec. 31, 1954. As seen from Table I, there were 18,261 deliveries during this period. The total number of cesarean sections performed was 739, or 4.04 per cent. The total number of twin deliveries in this group was 184, or one set in every 99.2 deliveries. Seventeen of these were delivered by cesarean section, which is an incidence of 9.2 per cent.

Table I. Incidence of Cesarean Sections in All Deliveries and in Deliveries of Twin Pregnancies

	NUMBER	INCIDENCE
Total No. of deliveries	18,261	
Twin deliveries	184	1:99.2 deliveries
Sections in entire series	739	4.04 per cent
Sections in twin deliveries	17	9.2 per cent

The description of the seventeen cases of twins delivered by cesarean section is found in Table II.

TABLE II. CASES OF MULTIPLE PREGNANCY DELIVERED BY CESAREAN SECTION

GRAVIDITY	PARITY OPERATION	INDICATION	TWIN A	(GRAMS)
iii	3/28/49	Repeat cesarean section	2,550	2,500
0	5/ 6/50	Pre-eclampsia; elderly primigravida	2,800	3,000
0	5/12/50	Contracted pelvis; fracture angulation of coccyx	2,250	2,300
•	1/14/51	Central placenta previa	2,000	1,900
•=	4/ 6/51	Face presentation with prolapse of hand; cervical dystocia; membranes ruptured over 24 hours; extraperitoneal section	2,450	2,350
iv	6/23/51	Third repeat section	2,350	1,800
0	7/29/51	Elderly primigravida; uterine inertia; overriding head; pre- eclampsia, moderately severe; membranes ruptured for 30 hours; extraperitoneal cesarean section	2,650	1,600
ii	8/17/51	Uterine inertia	2,500	2,900
	6/10/52	Tremendous varicosities of vagina and vulva	2,700	2,400
.,-	5/26/53	Placenta previa, eight months' gestation	2,300	2,000
•==	7/ 4/53	Repeat cesarean section	2,700	800
•=	12/ 2/53	Cephalopelvic disproportion; second twin delivered by esarean section 18 hours following delivery of first by low forceps	3,600	3,450
0	12/ 9/51	Contracted pelvis (flat rachitic type); pre-eclampsia; membranes ruptured over 24 hours; presenting part above brim; no labor pains	2,150	2,600
0	6/30/51	Elderly primigravida; uterine inertia after 6 hours of labor; ruptured membranes over 24 hours	2,300	1,900
ij	3/10/51	Placenta previa	1,400	1,500
0	3/ 1/50	Ovarian cyst, fixed, obstructing pelvis, not recognized during pregnancy	800	2,850
0	6/ 1/53	History of sterility; marked edema with hydramnios; multiple myomectomy one year before; x-ray showed one normal fetus and another congenitally deformed with absence of shoulder girdle		

Table III shows the indications for cesarean section in the 17 cases of twins.

TABLE III. INDICATIONS FOR SECTION*

	Cephalopelvic disproportion	4
	Previous cesarean section	3
	Placenta previa	3
	Uterine inertia	3
•	Cervical dystocia	1
	Pre-eclampsia	2
	Elderly primigravida	2
	Blocking of pelvic exit by tumor	1
	Presence of large monster	1
	Compound presentation	1
	Varicosities of vagina and vulva	1

*The number of indications exceeds the total number of cases because, as seen in Table II, there was more than one indication for section in some of the patients.

Four of these cases are of sufficient clinical interest to warrant more detailed description.

Case 1.—B. M. (No. 8552), a 28-year-old white primipara, had her last menstrual period on April 5, 1951. Her expected date of delivery was Jan. 10, 1952. She was admitted to the hospital on Dec. 8, 1951, at 7 A.M. with a history of rupture of the membranes during the night. About five days prior to admission, the patient developed a moderate swelling of both lower extremities. The blood pressure rose from 120/80 to 140/90 mm. of mercury. The urine showed 3 plus albumin. Her condition failed to improve in spite of rest in bed, sedation, and diuretics.

A roentgenographic study of the abdomen and pelvis showed the presence of twins. The measurements showed the pelvis to be of the flat rachitic type. The anteroposterior diameter at the inlet measured 8 cm. All the other dimensions of the pelvis were within normal limits.

The patient was kept in bed. She was given sedation, magnesium sulfate, and 10 per cent glucose in distilled water. On Dec. 9, 1951, the blood pressure was 140/90 mm. The edema of the ankles subsided somewhat. The urine showed 3 plus albumin. She had no labor pains. In view of the membranes being ruptured over 24 hours, the persisting toxemia, the presenting part remaining above the brim, the lack of labor pains, and the presence of a rachitic flat pelvis, it was decided to deliver the patient by cesarean section. Two female infants were delivered by a two-flap low cervical section. Baby A weighed 2,150 grams and Baby B weighed 2,600 grams. Mother and babies were discharged in good condition on the eighth postoperative day.

Case 2.—E. L. (No. 30339 U), a 25-year-old white woman, was admitted to the labor room on March 20, 1951, in active labor. The expected date of delivery was May 12, 1951. Multiple pregnancy was suspected but not confirmed by a roentgenographic examination. The membranes had been ruptured for 6 hours. Rectal examination showed the cervix to be about 3 cm. dilated and small parts were felt. This finding was interpreted as a double footling presentation. After 12 hours of labor, the cervix was found to be about 4 cm. dilated and the presenting part was a face in the left mentoposterior position with, in addition, a hand presenting. Because of the compound presentation of face and hand, the failure of the cervix to dilate beyond 4 cm. after 12 hours of labor, and the presence of ruptured membranes over 18 hours, an extraperitoneal cesarean section was performed. Two male infants were delivered. Baby A weighed 2,400 grams and Baby B weighed 2,500 grams. The postoperative course was uneventful.

CASE 3.—A. L. (No. 354480), a 34-year-old white woman, had her last menstrual period on Feb. 22, 1953. Her expected date of delivery was Nov. 29, 1953. In 1946, she had a normal spontaneous delivery of a 3,800 gram infant. A roentgenographic study on Oct. 26,

22

1953, showed the presence of a twin pregnancy. Both fetuses were in cephalic presentation, the head of one being at the brim of the pelvis, while the head of the other was to the left and higher, resting in the iliac fossa of the false pelvis.

The patient was admitted to the hospital on Dec. 1, 1953, and, after 16 hours of active labor, was delivered by midforceps of Baby A, who weighed 3,600 grams. The amniotic sac of Baby B was ruptured artificially about twenty minutes later. The patient continued to have labor pains about every 4 to 5 minutes. At the end of an hour of active labor, the head failed to enter the pelvis and remained above the pelvic brim. Three attempts were made to force the head into the pelvis by abdominal pressure from above, and to apply forceps to the presenting part. Each time the attempt failed. The shape of the head had a peculiar configuration to the examining hand of the operator, and the forceps could not be properly applied to fit the presenting part. A congenital anomaly was suspected. A roentgenographic study of the pelvis showed the head at the brim and no evidence of any definite deformity.

Twelve hours after delivery of Baby A, the head was still high, unengaged, and the fetal heart tones of good quality. A two-flap, low cervical section was then performed. A male infant, weighing 3,450 grams, was delivered. There was a single placenta.

The infant's head had an indentation in the right parietal and frontal region, forming a flattening of the dome of the skull. Both frontal bones were very prominent. This flattening of the dome of the skull resulted in a lengthening of the occipitofrontal and biparietal diameters, measuring 12.5 and 11 cm., respectively. This shape and configuration of the presenting part made it impossible for it to come through the brim of the pelvic inlet. This flattening was probably caused by the intrauterine pressure upon the skull against the bony parts of the pelvis. This pressure was further aggravated during the sixteen hours of labor preceding the delivery of Baby A.

CASE 4.—P. T. (No. 15449*), a 41-year-old Negro primigravida, was admitted to the hospital on June 1, 1953, complaining of shortness of breath and marked swelling of the abdomen and both lower extremities. The expected date of delivery was June 27, 1953. During September, 1951, the patient had had a multiple myomectomy, following a complaint of abdominal pains and a history of sterility of fifteen years' duration. Her antenatal course was uneventful until six weeks prior to her admission to the hospital. At that time, she developed edema of the lower extremities. The swelling became progressively worse in spite of sedation, rest in bed, and a salt-free diet. At no time was there any elevation of the blood pressure above 130/80 mm., or any proteinuria. Upon admission to the hospital, the abdomen was markedly distended, tense, protruding in both flanks, with the skin shiny from being overstretched. There was 4 plus pitting edema of both lower extremities and the lower back.

A roentgenographic study of the abdomen showed one fetus in the left occipitoposterior position, unengaged. There was another fetus with a congenital deformity, the shoulder girdle being absent. The diagnosis was that of hydramnios and twins, with one of the twins congenitally deformed, or a monster. In view of the age of the patient, the history of sterility, the previous myomectomy, the hydramnios, and the presence of the monster which it was thought might complicate the delivery of the apparently normal fetus, delivery by cesarean section was decided upon. A two-flap, low cervical cesarean section was performed. Baby A was a monstrosity with no shoulders or arms and was hard and stiff due to marked edema. Baby B was a normal female infant that weighed 2,800 grams.

The mother and baby were discharged on the ninth postoperative day in good condition.

Comment

As seen from Table I, the cesarean section rate in the hospitals from which this series was collected was 4.04 per cent. This compares favorably with the section incidence in the large maternity centers, which is 6.2 per cent, while

^{*}This case is being reported in greater detail by Dr. M. Silber, to whom I am grateful for permission to include it in this series.

d

the incidence in large hospitals throughout the country varies from 0.5 per cent to 14 per cent.⁴ In the two institutions concerned, the approach toward the problem of delivery by the abdominal route was a conservative one.

It was rather surprising, therefore, to find the incidence of cesarean sections in twin pregnancies to be 9.1 per cent, or more than twice the incidence for the entire group. While this series may be considered too small to be of any statistical significance, it is interesting to note that Potter and Fuller⁵ reported 15 cesarean sections in 252 twin deliveries, an incidence of 5.9 per cent, in the Chicago Lying-in Hospital for the period of 1941–1947. The over-all incidence of sections in the same institution for the period of 1941–1945 was 4.3 per cent. These authors listed the indications for the cesarean sections in these 15 cases as follows: previous cesarean section, 6; pre-eclampsia, 2; placenta previa, 2; elderly primigravida with fibroids, 1; elderly primigravida with hypertensive toxemia, 1; hypertensive toxemia with chronic renal disease, 1; essential hypertension, 1; twenty-four hours in labor without progress, 1.

A study of the indications in the present report for the delivery of the twins through the abdominal approach is of some interest. In patients with multiple pregnancies, in whom the uterus is usually overdistended, the danger of rupture following a previous section may be greater than in a patient with a single pregnancy, and one would, therefore, be justified in doing a repeat cesarean section in such a case. This was done in three patients of this group.

It is almost universally agreed that in cases of total, and in some instances of partial, placenta previa, cesarean section is the safest method of delivery. This indication applies equally in multiple as in single pregnancies.

Uterine inertia and cervical dystocia may conceivably occur as often, or even more frequently, in multiple pregnancies as in single ones. The uterine musculature in the former is usually overdistended and contracts poorly and irregularly. When the infants are large and the uterus overdistended and tense, inertia may set in. In a case of this type, one hesitates to use Pituitrin to overcome the inertia. If labor fails to progress after an adequate trial, delivery by section may be the solution. Similarly, in the case of cervical dystocia, with a compound presentation of face and hand, the most logical approach for delivery is the abdominal route.

Of special interest are the cases of cephalopelvic disproportion. The indications for section in Case 1 were several: pre-eclampsia, ruptured membranes for over twenty-four hours, with the presenting part floating above the pelvic brim. The fact, however, that the patient had a flat, rachitic pelvis, with an anteroposterior diameter of the inlet measuring only 8 cm., was a major contributing cause for the section.

The very presence of twins may cause cephalopelvic disproportion. This is illustrated in Case 3. In this case, the uterus contained two large infants whose combined weight was 7,050 grams. In addition to these, there was present a placenta and amniotic fluid in two separate sacs. One may assume that there was an extraordinary degree of intrauterine pressure. This intrauterine tension may have been great enough to exert sufficient pressure upon

the skull of Baby B, which was seen in the roentgenogram to be resting against the bony part of the false pelvis, to flatten the dome. As a result of this flattening, the presenting head became sufficiently deformed to prevent its passage through the pelvic brim.

It is known that intrauterine pressure may cause congenital deformities.7 Among them, asymmetry of the head and face and grooving of the skull are Many of these deformities will correct themselves without quite common. treatment. This applies especially to asymmetries of the head.⁸ In the case of Baby B, the flattening of the head cleared up almost completely on the sixth day. This was further proof that the malformation was temporary, due to intrauterine pressure.

Case 4 proves the exception to the rule. Greenhill⁹ stated, as one of the contraindications to cesarean section, the known presence of a monster. this case, however, one of the indications for the section was the fear that the monster might interfere with the delivery of the normal infant. This infant was especially valuable because the mother was a primigravida 41 years of age with a history of a long period of sterility. In retrospect, this monster could not have been delivered vaginally without great difficulty due to its abnormal size, shape, and the hardness of its tissues.

Summary

- 1. The incidence of cesarean section in cases of twins may be the same and even greater than that in cases of single pregnancy.
 - 2. The indications for delivery of twins by cesarean section are discussed.
- 3. It is suggested that uterine inertia and dystocia, due to overdistention of the myometrium, may occur frequently in multiple pregnancy and become a contributing indication for delivery by cesarean section.
- 4. Cephalopelvic disproportion proved to be a frequent indication in this series for delivery by the abdominal route. In one case the second twin had to be delivered by cesarean section because of cephalopelvic disproportion.

References

- 1. Lull, C. B.: Am. J. Obst. & Gynec. 46: 314, 1943.

- Lun, C. B.: AM. J. OBST. & GYNEC. 46: 314, 1945.
 Zettelman, J. J., and Bowers, V. M.: AM. J. OBST. & GYNEC. 65: 953, 1953.
 Irving, F. C.: AM. J. OBST. & GYNEC. 50: 660, 1945.
 Colvin, E. D.: AM. J. OBST. & GYNEC. 64: 473, 1952.
 Potter, E. L., and Fuller, M.: AM. J. OBST. & GYNEC. 58: 139, 1949.
 DeLee, J. B., and Greenhill, J. P.: Principles and Practice of Obstetrics, ed. 10, Philadelphia, 1951. W. B. Saunders Company, p. 444
- delphia, 1951, W. B. Saunders Company, p. 444.

 7. Chapple, C. C., and Davidson, D. T.: J. Pediat. 18: 481, 1941.

 8. Holt, L. E., and McIntosh, R.: Pediatrics, New York, 1953, Appleton-Century-Crofts, Inc., p. 102.

 9. Greenhill, S. P.: S. Clin. North America, 33: 87, 1953.

642 EASTERN PARKWAY

RUPTURE OF THE GRAVID UTERUS

A Ten-Year Survey

FREDERICK J. MAISEL, M.D., BALDWIN, N. Y.

(From the Obstetrical Service of the Nassau Hospital, Mineola, New York)

THE addition of this report to the many already in the literature may be justified by the following objectives: (1) to depict the experience in a general hospital in a rapidly growing suburban community as opposed to the large urban clinic, (2) to inquire whether there is a real increase in the incidence of rupture of the uterus in recent years, and (3) to contrast the maternal mortality in the eras before and after the establishment of a blood bank within the hospital.

It was decided that an arbitrary ten-year period, 1945-1954, would serve our purpose for several reasons. Complete case records were not available for the years prior to 1953. There were no ruptures of the uterus recorded for the years 1943 and 1944 (2,721 deliveries). We could be certain of the accuracy of the indexing of cases by diagnosis and operation after the year 1944. Also, these ten years coincided with the rapid influx of population and doubling of the number of deliveries per year.

From Jan. 1, 1945, through Dec. 31, 1954, there were 21,209 deliveries. There were 11 ruptures of the gravid uterus, an incidence of 1:1,929. It should be noted that the ruptures here reported are "gross ruptures" and do not include incomplete ruptures discovered at cesarean section. During these ten years there is no record of the diagnosis of rupture of the uterus having been made incorrectly, i.e., the diagnosis made, the patient operated upon, and no rupture found.

Our incidence of rupture of the uterus approximates that of three of the most recent reports available to us, as is shown in Table I. All attempts to determine whether there is an actual increase in gross rupture of the uterus from the reports in the literature were inconclusive, since most of the reports concern series of cases, not intervals of time. Analysis of our experience (Table II) was inconclusive, as we have too few cases. Comparison of the two five-year periods suggests a slight increase in the second five-year interval. The reason for attempting to determine whether there is an actual increase in rupture of the uterus, or not, will be discussed later in this paper.

The maternal mortality associated with rupture of the uterus as reported in the literature varies widely with the individual series. The older reports averaged 55 to 85 per cent. A more recent review by Eastman³ indicates a rate of 42 to 53 per cent. Ingram, Alter, and Carter's report shows a further lowering of the mortality rate to 35 to 40 per cent. Our maternal mortality was

27.2 per cent for the ten-year period. Table II demonstrates that our low mortality rate is due to the loss of but one patient after the establishment of the blood bank.

The infant mortality rate associated with rupture of the uterus as reported in the literature remains close to 80 per cent.³ Recent reports do no show any improvement comparable to the lowered maternal mortality. Our fetal loss was 81.6 per cent for the ten-year period. Table II shows a slight increase in our infant mortality for the second five-year interval. Due to the nature of rupture of the uterus and its implications for the fetus, any improvement in fetal mortality must be sought by avoiding rupture of uterus.

Our three maternal deaths illustrate certain important causes of uterine rupture, and emphasize the necessity of prompt and adequate treatment once rupture has occurred. They are presented in abridged form.

TABLE I. RUPTURE OF THE UTERUS

			TOTAL	R	UPTURES
AUTHOR	INSTITUTION	YEARS	DELIVERIES	NO.	INCIDENCE
Brierton ¹	Bellevue Hospital	1932-1946	111,753	57	1:1,961
Ingram, Alter, and Carter	Duke Hospital	7-1950	16,654	13	1:1,281
Hammerschlag (personal communication)	Harlem Hospital	1937-1954	55,192	20	1:2,759
Total			183-599	90	1:2,040
Maisel	Nassau Hospital	1945-1954	21,209	11	1:1,929

TABLE II. INCIDENCE OF RUPTURE OF THE UTERUS IN TEN-YEAR PERIOD AT NASSAU HOSPITAL

YEAR	NUMBER OF DELIVERIES	NUMBER OF CASES OF RUPTURE	INCIDENCE	MATERNAL DEATHS	FETAL DEATHS
1945	1,379	2	1: 689	2	1
1946	1,586	0	Blood bank est	ablished	
1947	1,652	0			
1948	1,642	1	1:1,642	0	1
1949	2,023	1	1:2,023	1	1
First 5 years	8,282	4	1:2,070	3 (75%)	3 (75%)
1950	2,148	0			
1951	2,388	1	1:2,388		1
1952	2,882	1	1:2,882		1
1953	2,863	3	1: 956		2
1954	2,646	2	1:1,323		2
Second 5 years	12,927	7	1:1,848	None	6 (85%)
10 years	21,209	11	1:1,929	3 (27.2%)	9 (81.6%

Case Reports

CASE 1.—A 34-year-old gravida iv, para ii, at 36 weeks' gestation, with a known breech presentation, after seven hours of ruptured membranes and five hours of labor, was noted to have a prolapsed cord. The infant was delivered by breech extraction through an incompletely dilated cervix. There followed immediately profuse hemorrhage and moderately severe shock. A diagnosis of ruptured uterus was made within thirty minutes; supracervical hysterectomy was begun two and a half hours after delivery. Supportive therapy was started five minutes after the hemorrhage and included 500 c.c. 5 per cent dextrose, 750 c.c. plasma, and 500 c.c. blood. The mother died six hours after delivery and three and a half hours

after operation because additional blood was not obtainable. The infant survived and is well. The conclusion of the staff conference was that there was an error in judgment in performing breech extraction through an incompletely dilated cervix, and that death was due to the fact that additional blood was not available in time.

Case 2.—A 37-year-old gravida iv, para i, at 40 weeks' gestation, was taken to the delivery room after four hours of normal labor because the usual "bloody show" suddenly became more profuse. Vaginal examination revealed a right occipitoposterior presentation at mid-station with a 1 cm. rim of cervix. The membranes were ruptured artificially at this time. The patient remained on the delivery table with the obstetrician in attendance. One hour after rupture of the membranes sudden profuse vaginal hemorrhage and severe shock were noted and the diagnosis of ruptured uterus was made. Supportive therapy had been started 30 minutes before the hemorrhage and included 1,000 c.c. 5 per cent dextrose, 750 c.c. plasma, but no blood because she died (undelivered) within 30 minutes as she was being placed on the operating table. The diagnosis of ruptured uterus was confirmed by manual exploration after death. Her first delivery (at another hospital) was said to have been terminated by high forceps. We may conclude that this case is an illustration of "silent" rupture during normal labor due to probable trauma in a previous delivery. The conclusion of the staff conference was that, had our delivery room been equipped for immediate laparotomy, this patient would have had a better chance for survival.

CASE 4.—A 28-year-old gravida i, para 0, at 42 weeks' gestation, had a fully dilated cervix after thirty hours of labor. She was taken to the delivery room and a Kielland forceps rotation from right occipitoposterior was attempted. Rotation could not be accomplished. Upon removal of the forceps the cord prolapsed. Podalic version and breech extraction were performed with Piper forceps to the aftercoming head. Signs of shock were noted upon delivery of the baby, cyanosis and rapidly falling blood pressure, followed by circulatory collapse. There was very little external bleeding. The diagnosis of ruptured uterus was made at this time. Attempts to establish venoclysis failed, since all accessible veins were collapsed. A "cut-down" was not done. The mother died one hour after delivery; the infant died 15 minutes after birth. The diagnosis was confirmed by manual exploration after death. Death was attributed to the rapid circulatory collapse and failure to establish venoclysis. The conclusion of the staff conference was that had our delivery room been equipped for immediate laparotomy, had an intravenous pathway been established before attempting version and extraction, this patient would have had a better chance for survival.

The possible error in judgment in doing a version and extraction in a primipara for prolapsed cord is not pertinent to this paper.

Comment

1. Our experience in a rapidly growing community indicates that with the increasing delivery rate there will be an increasing number of ruptures of the uterus, while the incidence remains about the same. If the maternal mortality rate of a hospital with a rapidly expanding obstetrical service is not to be adversely affected, attention will have to be directed toward the prevention of rupture of the uterus, its prompt diagnosis, and prompt and effective management. Concerning prevention, our experience (Table III) included 6 cases that may be classified as beyond our control. The remaining 5 cases (almost one-half) in which rupture of the uterus might have been avoided, included 2 (of 3) maternal deaths, and 3 (of 9) infant deaths. Four of these 5 ruptures of the uterus were associated with breech extraction, 2 has a partial deaths, 2 done deliberately and carefully. Only one of these patients was a nullipara, 4 may well have had "unrecognized, asymptomatic, partial

TABLE III. TEN-YEAR EXPERIENCE WITH RUPTURE OF THE UTERUS AT NASSAU HOSPITAL

									THERAPY					
											TIME OF		OUTCOME	OME
YEAR	CASE NUM- BER	AGE	GRAVID- ITY	PAR-	WEEKS' GESTA- TION	WEEKS' GESTA- HOURS' TION LABOR	CAUSE OF RUPTURE	5% GLU- COSE (C.C.)	PLASMA BLOOD (C.C.)	BLOOD (C.C.)	PROBABLE RUPTURE TO OPER- ATION	HYSTER- ECTOMY	MOTHER FETUS	PETUS
1945	-	34	iii	ii	36	5	Breech extraction for prolapsed cord	200	750	200	2 hours	+	D	A
1945	63	37	i	•	40	4	Occult rupture during labor, died in 30 minutes undelivered	1,000	750	0		0	D	D
1946	1	1	1	1	1	ı	Blood bank established (Feb.)	1 1 2 1	1	1		1	1	1
1948	ಣ	36	ii		24	0	Interstitial pregnancy; ectopic "sus-	1,000	750	1,000	1,000 12 hours	+	A	D
1949	4	88	epril	0	42	30	Failed forceps, prolapsed cord; version and extraction	0	0	0		0	О	D
1921	2	. 35	ii		32	0	Previous classical cesarean section	1,000	0	2,000	54 hours	+	A	D
1952	9	27	ii		36	0	Previous classical cesarean section	1,000	0	2,500	2 hours	+	A	D
1953	L -	35	iii	::	40	9	Arrested brow presentation; version and extraction	1,000	0	2,000	35 min- utes	+	A	D
1953	00	88	iv	ij	40	24	Arrested breech presentation; breech extraction	1,000	200	3,000	2 hours	+	A	A
1953	6	23	i	iii	40	14	Desultory labor, Pitocin infusion, Kielland forceps	100	750	2,500	2,500 45 min- utes	+	A	D
1954	10	43	ij		36	0	Previous classical cesarean section	1,000	0	2,000	2,000 11 hours	+	A	D
1954	11	36	iii	:I	42	6	Occult rupture, not diagnosed	1,000	0	1,000	6 hours	+	A	Q

ruptures in a previous pregnancy' as emphasized by Standard, Philipp, and Webster, who point out that the multipara who has a prolonged labor, with or without an unfavorable presentation or position of the fetus, may be a likely candidate for rupture of the uterus.

Concerning prompt diagnosis, one consideration is of paramount importance: constant awareness of the possibility of ruptured uterus, especially in any delivery considered to be even slightly traumatic, with immediate digital exploration of the cervix and uterus to establish or rule out the diagnosis.

Concerning prompt and adequate treatment, our experience gives precedence to the availability and use of large quantities of whole blood as indicated. Of equal importance is the establishment of an intravenous pathway. Since our experience with Case 4, it is our practice to insert a large intravenous needle before attempting any potentially traumatic procedure, or immediately upon noting more than usual bleeding, whether this occurs before, during, or after delivery. Not shown in the tables are other important reasons for our lowered mortality: the prompt, efficient, and careful work of the laboratory staff in cross-matching and supplying whole blood; the speed of the operating room staff in readying the operating room; the instant availability of trained anesthesiologists; all of which, fortunately, are the necessary concomitants of an increase in the work load of a modern hospital.

2. One of the objections to the increase in the cesarean section rate is the danger of the scar predisposing to rupture of the uterus in a subsequent pregnancy. This danger for the now largely discarded classical cesarean, was found, by Coleman,2 to have an incidence of 1:9,551 deliveries. Our incidence was 1:7,065 deliveries. Compared to our total incidence, the danger from traumatic delivery is over three times as great. The incidence of rupture of the cervical scar is very low as may be judged from the fact that (it is claimed) 1,000 cervical cesarean sections were performed at the Chicago Lying-in Hospital without a rupture occurring in a subsequent pregnancy. Therefore, with the advent of the almost universal performance of the cervical operation, the danger of rupture due to this factor will be much less than the danger inherent in a traumatic delivery. Unless it can be shown that rupture of the uterus is increasing due to the greater use of the cesarean section, evaluation of the risks of "difficult" delivery from below, with particular reference to the possibility of ruptured uterus, as opposed to those of cesarean section will, in certain cases, often "justify" the choice for cesarean section. Only avoidance of rupture of the uterus will improve the fetal mortality. Our most recent impacted brow presentation was delivered by cesarean section, when manual conversion to a vertex was unsuccessful, and forceps could not be applied.

Is the incidence of rupture of the uterus increasing? As already mentioned we were unable to determine this from the literature. Table II is presented in detailed form in the hope that others will depict their experience in similar tabulation. It would then be possible to assemble comparable data on a significantly large number of cases, and determine whether or not the higher cesarean section rate is actually contributing to the incidence of uterine rupture. If it is not, then the incidence of ruptured uterus may be safely reduced

by the judicious use of cesarean section, especially in multiparas who have a history of previous trauma, and have prolonged labors with unfavorable presentations and/or positions of the fetus.

3. The improvement in our maternal mortality rate after the establishment of a blood bank within the hospital has been mentioned, and needs no elaboration.

Summary

- 1. A ten-year survey of rupture of the gravid uterus in a general suburban hospital is presented.
- 2. An increase in the incidence of ruptured uterus could not be demonstrated, although the experience of the last two years strongly suggested such an increase.
- 3. Marked improvement in the maternal mortality rate is shown to be largely due to the establishment of a blood bank within the hospital.
 - 4. Clinical data on eleven ruptures of the uterus are presented in Table III.
 - 5. Abridged case reports of three maternal deaths are presented.

References

- Brierton, J. F.: Am. J. OBST. & GYNEC. 59: 113, 1950.
 Coleman, P. F.: Obst. & Gynec. 5: 773, 1955.
 Eastman, Nicholson J.: Williams Obstetrics, ed. 10, New York, 1950, Appleton-Century-Crofts, Inc.
- Ingram, J. M., Alter, R. L., and Carter, B.: Am. J. Obst. & Gynec. 64: 527, 1952.
 Lynch, F. J.: Am. J. Obst. & Gynec. 49: 514, 1945.
 Standard, J., Philipp, E., and Webster, A.: Obst. & Gynec. 4: 348, 1954.
- - 1 WESTMINSTER ROAD

BROW PRESENTATION*

LAWRENCE H. MADDEN, JR., M.D., PITTSBURGH, PA.

(From the Department of Obstetrics, Pittsburgh Hospital)

n

h

Ι.

BROW presentation is a formidable obstetric complication. The rarity of its occurrence limits the experience of each obstetrician. Hence, the formation of individual opinions regarding management must be based on small numbers of cases which cannot be statistically significant. The problem is accentuated by the scarcity of literature on this subject. Since 1925 three papers dealing with brow presentation have appeared in American journals and comparably few in the foreign literature.

A survey of 13,774 deliveries at Pittsburgh Hospital for the ten-year period from Feb. 1, 1945, through Jan. 31, 1955, disclosed 13 which persisted as brow presentations until the second stage of labor. These were studied with emphasis on the selected methods of management in relation to fetal and maternal results. In order to reach conclusions of statistical significance, these observations are combined with those of the several writers on this subject since 1925. These are Posner and Buch,² Hellman and associates,³ Morris⁴, and Kenwick.⁴ These authors combined their statistics on face and brow presentations so that it is impossible to make a comparison with any one series in all aspects of this problem. There are important differences in incidence, etiology, management, and clinical results between face and brow presentations. This series deals exclusively with the complications of the latter.

Incidence.—The reported incidence varies from 1:1,000 to 1:3,500. Table I shows an incidence of 1:1,816 in 270,641 deliveries in the reporting hospitals for periods varying from 10 to 50 years.

TABLE I. COMPARISON OF INCIDENCE IN RECENT REPORTS OF BROW PRESENTATIONS

	DELIVERIES	BROW PRESENTA- TIONS	INCIDENCE	RATE
Posner and Buch	46,058	13	0.028	1:3,543
Hellman and associates	69,930	44	0.060	1:1,498
Morris	64,817	53	0.080	1:2,224
Kenwick	76,062	26	0.034	1:2,941
Author	13,774	13	0.090	1:1,059

Etiology.—Both fetal and maternal factors have been cited as causative. All other authors note a high incidence of pelvic inlet contraction. Hellman reported (in both white and Negro patients) a percentage of 57.9. In our series only one case of contracted pelvis was noted. Hellman and Kenwick have both considered grand multiparity as a factor in incidence. In the series of 13 cases herein reported, 6 patients were multiparas, one in her eighth pregnancy. Atonicity of the abdominal wall and pelvic diaphragm resulting in faulty uterine

^{*}Presented at a meeting of the Pittsburgh Academy of Medicine, March 8, 1955.

axis had been implicated as the extension mechanism in multiparas in contradistinction to the unyielding tissues of the primigravida which at times are the cause of failed flexion. Hellman found 37.2 per cent primigravidas in his series. In our series 55.5 per cent were primigravidas which agrees more closely with Morris' 62 per cent. The age of the mother has apparently little effect upon the frequency of brow presentations. The literature and our series failed to disclose any age group in which this type of presentation was predominant. In one case a large fibroid had apparently interfered with the normal mechanism. A placenta in the lower segment might behave similarly. Early rupture of the membranes has been considered as of possible etiological significance. This occurred in 23 of the 53 cases reported by Morris. Rupture preceding delivery by more than eight hours occurred in only 2 of our cases. Fetal size, either above average or unusually small, as in prematurity, may be responsible for faulty mechanism. Basically this means that there is cephalopelvic disproportion. In Morris' group 31.3 per cent, and in our own 30.7 per cent weighed more than 8 pounds. The smallest infant weighed 5 pounds, 13 ounces. Fetal anomalies, multiple pregnancies, hydramnios, prolapsed cord, or loops of cord around the neck acting as a tumor have been considered in the etiology but were not found in this survey.

Diagnosis.—Early diagnosis (before the beginning of the second stage) is made in about half the cases; in Morris' group 26 of 53, or 49 per cent, and in our own 7 of 13, or 53 per cent. This failure in early diagnosis is noted also in combined reports of face and brow presentations. Careful use of the facilities at hand, i.e., proper abdominal palpation and auscultation, judicious internal examination, and more frequent roentgen examination in prolonged labor will facilitate early diagnosis and improve results.

Labor.—Labor is usually prolonged. The lower uterine segment is not symmetrically filled and inertia is the rule. The facial bones mold less readily to the pelvic contour and the expulsive forces are ineffective. The greater diameters of the extended head contribute to unsatisfactory descent. The second stage is slow and often associated with complete arrest. In Morris' series 38.5 per cent of the primigravidas had a second stage of longer than 2 hours. In his combined face-brow series, Kenwick reported prolongation of labor in 18.4 per cent of primigravidas and 26.4 per cent of multigravidas. In our series there were 4 cases of prolonged labor, 3 in primigravidas, the longest being 45 hours, and one in a gravida viii in whom the first stage lasted 23 hours.

Management of Delivery .-

1. Spontaneous or elective low forceps. Five patients were delivered by these procedures. Three of the 5 presentations were converted by flexion and 2 were extended and delivered as face presentations. This is a percentage of 38.5 as compared to Posner and Buch's 17 and Hellman's 31.1 per cent. These authors reported 50 and 7.1 per cent fetal mortality, respectively. There were no fetal deaths in this group in our series.

2. Operative procedures from below. Flexion by manipulation was attempted in 3 cases. It was unsuccessful in one, the head later extending completely and being delivered spontaneously. This is included in the first group. In 2 other cases the maneuver was successful and delivery was completed by midforceps. One fetus perished intra partum. Six patients were delivered by internal podalic version and breech extraction with one neonatal death after fifteen hours. The group incidence is 61.5 per cent with a fetal mortality of 25.0 per cent. Hellman's incidence of operative obstetrical deliveries was 40 per cent with a fetal loss of 50 per cent, while Posner and Buch listed 66 per cent and 18 per cent, respectively.

3. Cesarean section. There were no sections for brow presentations at Pittsburgh Hospital. In Hellman's series, 35 per cent were delivered abdominally with a fetal mortality of 45 per cent, whereas Posner and Buch had an incidence of section of 17 per cent with no fetal mortality. These figures indicate the futility of comparing statistics with such a small number of cases.

Maternal Morbidity and Mortality.—There was no significant maternal morbidity in our group or in the others which were studied. Hellman reported 3 maternal deaths. Two of these were neglected cases and the third patient died following cesarean hysterectomy.

Comment

The etiological factors which result in brow presentations are variable and relatively obscure. Earlier diagnosis in a higher percentage of cases together with efficient management by competent obstetrical operators offers the best hope for improvement in our results in this difficult condition. The former objective can be accomplished by careful and more frequent use of available methods. Management after diagnosis will be variable, depending upon the stage of progress at the time and the skill and experience of the attendant. The absence of fetal loss in our series and the 7.1 per cent infant mortality reported by Hellman in cases of spontaneous or elective low forceps delivery indicate this method to be desirable if possible. Higher fetal wastage is inevitable when active operative interference from below must be employed. Greenhill contends that most brow presentations diagnosed early in labor will spontaneously convert to a vertex or face presentation and labor should be permitted to progress without interference. In Morris' series 13.2 per cent, in Hellman's 31 per cent, and in our own 23 per cent converted spontaneously and were easily delivered with low fetal mortality. Our good fortune in obtaining 5 healthy babies in 6 cases of internal podalic version and extraction has not been duplicated in other reports. Forceps delivery above the outlet level with an extended head is hazardous for the fetus. Operative delivery of brow presentations from below should probably be undertaken only in cases where progress is arrested, when the most favorable conditions obtain, when there is no question of disproportion, and only by skilled, experienced operators. For the remainder, especially in primigravidas, cesarean section should be more often utilized.

Summary

- 1. Thirteen cases of brow presentation from the obstetrical service of Pittsburgh Hospital have been studied, together with a review of the literature from 1925.
 - 2. The etiology is variable and relatively obscure.
 - 3. Earlier diagnosis is essential to improvement of final results.
 - 4. Management of this complication is outlined.

References

- 1. Morris, Norman: J. Obst. & Gynaec. Brit. Emp. 60: 44, 1953.
- 2. Posner, A. Charles, and Buch, Irwin: Surg., Gynec. & Obst. 77: 618, 1943.
 3. Hellman, L. M., Epperson, John W. W., and Connolly, Frank: Am. J. Obst. & Gynec. 59: 831, 1950.
- 4. Kenwick, Anthony: Am. J. OBST. & GYNEC. 66: 67, 1953.

SHOULDER PRESENTATION*

AUGUSTA WEBSTER, M.D., AND W. F. GEITTMANN, M.D., CHICAGO, ILL.

(From the Department of Obstetrics, Cook County Hospital, the Department of Obstetrics and Gynecology, St. Luke's Hospital, and the Department of Obstetrics and Gynecology, Northwestern University Medical School)

S HOULDER or scapula presentation is an obstetric problem that has plagued us with discouraging results. Hence, we have reviewed the records of this complication at the Cook County Hospital and St. Luke's Hospital, Chicago, for the five-year period of 1949 to 1953, inclusive, in an effort to evaluate the management of these patients in relation to both fetal and maternal salvage. During this time, there were 84 patients with shoulder presentation at Cook County Hospital and 16 at St. Luke's. We have limited this report to the transverse presentations occurring from the twenty-eighth week of gestation to term and have excluded twin pregnancies.

While there is no specific etiology for this condition, there are certain predisposing factors. Our material is comparable to that reported in other publications in that multiparity predominates (Table I). There were only 8 primiparas and the remainder or 92 were multiparas.

TABLE I. PARITY

]	PARITY								
	0	i	ii	iii	iv	v	vi	vii	viii	ix	X	xi	xii	xiii	xiv	xv	xv
Number	8	25	22	15	5	6	6	6	3	0	2	1	0	0	0	0	1

There were 25 patients (25%) with placenta previa. Other factors were fetal monstrosity, cervical fibroid, and 2 instances of abdominal pregnancy.

We divided our patients arbitrarily, according to the gestational period, into two groups. The first group of thirty-two weeks' gestation and under included most of the smaller babies. The second group of thirty-three weeks' gestation and older included the larger babies with a better chance of survival.

TABLE II. LENGTH OF PREGNANCY 32 WEEKS OR LESS

TYPE OF DELIVERY	NO. CASES	DEAD ON ARRIVAL	LIVE BIRTHS	TOTAL FETAL DEATHS
Braxton Hicks version	11	5	2	9
Version and extraction (1 with cranial decompression)	4	2	0	4
Corporis conduplicatio	1	1	0	-1
Voorhees bag	5			4
1 cesarean section			1	
2 corpore conduplicato		1		
1 Braxton Hicks version				
1 Braun's hook and decapitation				
Cesarean section	2		1	1
Total	23	9	4	19

^{*}Presented at a meeting of the Chicago Gynecological Society, April 15, 1955.

Table II shows the methods of delivery and the fetal mortality in 23 patients of thirty-two weeks' gestation and under. There were 11 instances of Braxton Hicks version, and 4 versions and extractions.

A Voorhees bag was used in 5 instances. A constriction ring developed in one of these patients and cesarean section was done with good results for both mother and baby. In 2 patients 10 cm. bags were used and small babies were delivered spontaneously corpore conduplicato when dilatation was complete. In one instance after the bag was expelled, a Braxton Hicks version was done and a spontaneous delivery occurred one hour later. The fifth patient in whom a Voorhees bag was used was delivered by Braun's hook and decapitation after the bag was expelled.

In this group of small babies, cesarean section was done as a primary procedure in 2 instances with one living infant.

The total fetal loss was 19, or 82.6 per cent, in this whole group. Nine infants were dead on arrival at the hospital, however, seven of the patients with absent fetal heart tones were bleeding from placenta previa or abruptio placentae, and 3 of these cases were further complicated by prolapse of the cord and an arm. The 2 others with fetuses dead on arrival had prolapsed cords.

Placenta previa occurred 13 times in the entire small group with many of the babies dead or in poor condition on entrance to the hospital. We believe that when the baby is already dead or previable, placenta previa should be treated conservatively and cesarean section should be avoided if possible. The most conservative method of delivery compatible with maternal safety is selected. In the absence of a total previa, we have found Braxton Hicks version very satisfactory for the management of placenta previa in the previable group.

Many patients entered the hospital with advanced cervical dilatation so that delivery from below was warranted.

Table III shows the fetal mortality and various types of delivery in the gestations of thirty-three weeks to term. Cesarean section and version and extraction were the most frequent methods of delivery. The fetal survival was 81.58 per cent when cesarean section was done. Two of these babies were dead on admission, one from ruptured uterus. The second known dead baby was delivered by section because a cervical fibroid obstructed the birth canal. When correction is made for these 2 babies who were dead on admission, the survival in the section group is 86.9 per cent. It must be recognized, however, that cesarean section was performed when optimum fetal results were expected. These cases were, for the most part, diagnosed early in labor and the babies were in good condition.

TABLE III. LENGTH OF PREGNANCY 33 WEEKS TO TERM

TYPE OF DELIVERY	NO. CASES	DEAD ON ARRIVAL	Т	OTAL FETAL DEATHS
**Cesarean section	38	2		7
*Version and extraction	24	4		11
*Braxton Hicks version	2			1
External version	2			0
Voorhees bag	2			1
Willett forceps to scalp	2			2
Conduplicatio corporis	3	2		3
Maneuver of Douglas	1			1
*Embryotomy	1	1		1
Abdominal pregnancy	2	1		2
Total	77	10		29

^{*}The five ruptured uteri are indicated by the 5 asterisks.

The procedure of choice was version and extraction in 24 cases in which labor was well advanced and conditions were favorable for prompt delivery on arrival at the hospital. Four of these patients had dead babies, were ready to deliver, and had had ruptured membranes from twenty-four hours to eight days when admitted. Five more of these patients lost their babies intranatally. Three had prolapsed arms or cords, however, and 2 of these had partial placenta previa with brisk bleeding. There were also 2 postnatal deaths, both in babies with a prolapsed arm before entrance to the hospital. It must be emphasized that all of these patients were far advanced in labor and cesarean section was contraindicated.

Braxton Hicks version was used only twice in the larger babies with the loss of one baby. The mother of the stillborn infant was a para viii, gravida ix, who arrived at the hospital in active labor, the cervix 3 cm. dilated, with irregular fetal heart tones and a prolapsed cord. During an attempt to replace the cord, the fetal heart tones disappeared and Braxton Hicks version was done. This procedure is fraught with such danger to the fetus that it is not used if the baby is viable and in good condition.

External version was used successfully only twice. This procedure is feasible only when the membranes are intact and the patient is not in labor or is in very early labor.

A Voorhees bag was also used twice with successful delivery of one living baby and one stillborn baby in a case where prolapse of the cord had preceded the introduction of the bag.

Willett forceps were used in 2 instances. An unregistered, unmarried 15-year-old gravida i entered the hospital in active labor, bleeding from a partial placenta previa. The head was brought over the inlet and the operator grasped the scalp with a Willett forceps. Gentle traction controlled the bleeding and delivery followed in a short time. The other was a case of hydrocephalus in which the head was grasped with a Willett forceps and a needle inserted to remove the fluid, after which traction was applied. The dead fetus was delivered after a seven-hour labor.

Three small dead babies were delivered by the maneuver of corporis conduplicatio and one by the Douglas maneuver.

There were 2 abdominal pregnancies in this series. Therefore, one must consider extrauterine gestation as a differential diagnosis when transverse presentation is found. This is especially true when the baby is shown lying high in the abdomen on flat plate x-rays. In both instances of abdominal pregnancy in this series, the patients complained of intermittent abdominal pain. In each case on sterile vaginal examination, the cervix was long and uneffaced, and the os was closed. In one of the patients the fundus was a ballotable mass just above the symphysis, and in the other there was a retropubic mass. Both patients were operated upon. Term infants were delivered that weighed 8 pounds, 13½ ounces, and 7 pounds, ¾ ounce, respectively. The placentas were left in place and adequate blood replacement was given. In one instance, 16 pints of blood was required and the patient made a complete though stormy recovery.

In this series there were 5 ruptured uteri. The first patient, a para viii, gravida ix, came to the hospital with the cord and an arm prolapsed in the vagina. Fetal heart tones were absent and the baby was delivered by decapitation. Exploration of the uterus showed a rupture of the lower uterine segment and a hysterectomy was done.

The second patient, a para ii, gravida v, was bleeding briskly on admission from a partial placenta previa. The cervix was 6 cm. dilated and an arm had prolapsed. A Braxton Hicks version was accomplished and extraction delayed

1

S

S

te

g

S

h

6

y

3-

n

d

until complete dilatation was present. The infant was living and weighed 5 pounds, 3 ounces. In the routine inspection following operative delivery, a cervical tear was found. This was sutured, but bleeding continued. Further investigation showed an extension of the cervical tear into the broad ligament and a hysterectomy was done.

The third patient had a ruptured uterus associated with version and extraction. She was a para i, gravida ii, and was admitted as an emergency. An arm was prolapsed through a completely dilated cervix and the patient was having such tumultuous contractions that the presence of fetal heart tones was questionable. The urgency of the situation offered no alternative other than immediate delivery by version and extraction under deep ether anesthesia. A nonmacerated stillborn infant was delivered. Intrauterine examination showed a rupture of the uterus and a hysterectomy was done.

The fourth patient, a para vii, gravida ix, arrived at the hospital in active labor with no symptoms of threatened rupture. The cervix was 7 cm. dilated and a hand had prolapsed. The baby was at term, fetal heart tones were present, and the maternal blood pressure was 130/80. A prompt cesarean section was performed. A tear in the lower uterine segment was found with a dead baby lying free in the peritoneal cavity. The uterus was removed.

The fifth instance of a ruptured uterus occurred in an obese patient, para ii, gravida iii, with pre-eclampsia and uncontrolled diabetes, whose obstetric condition was further complicated by a partial placenta previa and a temperature of 105° F. on admission. Fetal heart tones were never heard and excessive obesity (300 pounds) obscured the diagnosis of position. Efforts to induce labor with intravenous Pitocin did not produce either subjective or objective signs of labor. Vaginal examination then revealed a closed cervix and x-rays showed a transverse presentation. Inability to produce contractions combined with an increasing septic state and foul vaginal discharge, caused the obstetrician to whose service the patient was assigned to decide reluctantly to do a cesarean hysterectomy.

When the abdomen was opened a large tear was found in the lateral wall of the fundus and a macerated baby was free in the peritoneal cavity. Marked crepitus in the tissues suggested *B. welchii (Clostridium welchii)* infection. Antitoxin was given and the patient recovered. The time of the rupture was not determined, but the consensus was that a silent rupture had occurred before admission to the hospital and was the cause of the severe sepsis.

Summary and Conclusions

- 1. One hundred cases of shoulder presentation are reported. Placenta previa was present in 25 per cent of the patients; other predisposing factors were fetal monstrosities, cervical fibroids, and multiparity.
 - 2. There were no maternal deaths.
- 3. There were 2 abdominal pregnancies. This condition must be considered in the differential diagnosis of shoulder presentation.
- 4. Braxton Hicks version was performed 13 times and is a valuable procedure for delivery in the smaller or seriously jeopardized babies for the treatment of placenta previa.
- 5. Version and extraction were performed 28 times in patients whose labor was far advanced upon entrance to the hospital. There is great risk of rupture of the uterus in this procedure and extreme care must be used.

- 6. Cesarean section was performed 41 times. This procedure should be reserved for viable babies in good condition and all cases of total placenta previa.
- 7. A total of 48 babies was lost, 20 of whom were dead on arrival at the hospital, 17 died intranatally, and 11 died during the twenty-eight day neonatal period.
- 8. Successful management of shoulder presentation depends upon early and accurate diagnosis and the free use of cesarean section.

Discussion

DR. HENRY BUXBAUM.—Shoulder, or preferably transverse presentation, because the shoulder is not always the presenting part, is always a timely subject in spite of the rarity of its occurrence, because of the changing concept and improvement in the management of this form of dystocia.

Another etiological factor not mentioned by the authors is developmental anomalies of the uterus, such as arcuate and septate uterus. This condition is chiefly responsible for cases in which repeated malpresentations occur in subsequent pregnancies, and can be demonstrated clinically by uterine exploration or x-ray after intrauterine injection of an opaque medium.

The authors repeatedly demonstrate the hazards of the Braxton Hicks combined version. This is forcibly brought out by their own figures. They performed combined version 13 times in both series, in 5 of which the fetus was dead on arrival at the hospital. In the remaining 8, they had 5 perinatal deaths, a 63 per cent mortality rate..

At this time I wish to call your attention to their use of the word previable, in their first group of women from 28 to 32 weeks pregnant. These should have been classified as premature and not previable, which may have made a difference in the method of terminating these cases.

The use of the intrauterine bag has been relegated to antiquity, and rightfully so, but I can visualize a situation such as I once had where it could be employed, and that was a case of transverse lie in a patient in early labor with an anencephalic monster.

The authors also dramatically point out the ever-present possibility of rupture of the uterus in transverse presentation, especially when associated with placenta previa, 5 per cent in this series. This is readily apparent when we take into consideration the passive congestion in the lower pole of the uterus that is present in placenta previa, so that any vaginal manipulation may cause the cervix to tear like wet blotting paper with extension into the highly vascular lower uterine segment. Also the thinned-out lower uterine segment plus internal version or even combined version, which may precipitate tumultous uncontrollable uterine contractions, is certainly conducive to rupture of the uterus.

My whole discussion leads me to the conclusion that if the indications for cesarean sections are to be broadened, this is the place to start. I agree with the authors that cesarean section is the operation of choice in most cases of transverse presentation, premature or at term, primipara or multipara, membranes ruptured or intact, with 4 possible exceptions in the absence of total placenta previa. They are (1) complete or almost complete dilatation when the patient enters the hospital, (2) monstrosities, (3) absence of fetal heart tones, and (4) previable babies.

DR. A. J. KOBAK.—Persistent shoulder presentation is a problem that formerly taxed all the ingenuity of the well-trained obstetrician. The management of this problem depends upon when it is first recognized. In earlier pregnancy it is alleged to occur more frequently, but spontaneous rectification often occurs at this time. Before the onset of labor, or even early in labor with the membranes still intact, a Wigand type of external version can easily correct this abnormal presentation. The authors mention only two instances wherein this has been resorted to, but the source of material for this study was

f

f

from persistent transverse presentations that were found in the labor room. It is quite possible that an unknown number of external versions performed in the outpatient clinics might not have been known to them if they did not revert to a transverse presentation.

The study of shoulder presentation by Drs. Webster and Geittmann indicates that the management of this abnormal presentation is entirely different from the accepted plan of therapy of a generation or more ago. The strategy of management at that time was to plan upon a version and extraction. In order to facilitate this procedure we used to insert a Voorhees bag extraovularly within the cervix. This was done early in labor to prevent premature rupture of the membranes. It was of such size that its expulsion would find the cervix completely dilated and the bag of waters still intact, thus providing optimum conditions for a version and extraction. It is very gratifying that we have discontinued this procedure because the fetal mortality was too high. A cesarean section in those days was regarded to be a very dangerous procedure and was reserved more for cases of disproportion, and, if performed after prolonged rupture of membranes, the uterus was prophylactically removed to avoid postoperative sepsis.

In view of the present-day safety of the cesarean section, even in the presence of sepsis, and in view of the very high fetal mortality when these mothers are subjected to a vaginal delivery, it is obvious that the present trend toward cesarean section as the choice of treatment is a correct one. To obtain a greater fetal salvage through cesarean section, it is necessary to perform this operation as early in labor as is possible. This is not easily done. Many of these patients at the Cook County Hospital, as well as other institutions that have a large clinic service, arrive at the hospital with "dead on arrival" babies. Also because of the multiparity of a large proportion of the patients, they may be farther advanced in labor when they are first seen in the labor rooms, and the condition of the baby because of earlier rupture of the membranes or prolapsed cord may be poor, so that a vaginal delivery is regrettably the only procedure that can be done under the circumstances.

There still remain a number of patients with transverse presentation who arrive at the hospital sufficiently early for a cesarean section but this is not done because the diagnosis of shoulder presentation was not made. A careless routine "rectal" too frequently misses the real problem until too late for the preferred cesarean section.

I would like, therefore, to recommend more vaginal examinations, especially when the rectal examination is inconclusive; and whenever a breech is believed to be the presenting part, a vaginal examination might reveal that a baby's hand was felt instead of its feet. The authors have clearly shown that cesarean section is preferred, and the last item in their summary should never be forgotten—"Successful management of shoulder presentation depends upon early and accurate diagnosis."

THE METABOLISM OF URATE IN PRE-ECLAMPSIA*

JOSEPH SEITCHIK, M.D., PHILADELPHIA, PA.

(From the Divisions of Women and Biological Chemistry, Hahnemann Medical College, and the Philadelphia General Hospital)

THE plasma urate concentration is often elevated in severe acute toxemia of pregnancy, and the presence of hyperuricemia is suggestive of a poor fetal prognosis.¹ Therefore, investigation of the metabolism of urate in normal pregnant women and in patients with pre-eclampsia seemed worth while, and such studies were initiated in our laboratory about four years ago.²

At the beginning, we repeated Dr. Chesley's^{3, 4} investigation of the renal excretion of uric acid, and confirmed his observations that the renal tubular reabsorption of urate was increased in about 80 per cent of the patients with acute toxemia of pregnancy, that this abnormality of renal function appeared prior to or with the onset of the clinical syndrome, and that the percentage of urate reabsorbed from the glomerular filtrate bore no proportionate relationship to the severity of the disease. It seemed obvious from these studies that, if the renal tubular reabsorption of urate did not increase with increasing severity of the disease, some other factor, such as increased production or decreased destruction of urate, must be responsible for the frequency of hyperuricemia in the severe cases of pre-eclampsia.

Unfortunately, information concerning uric acid metabolism in toxemic women is meager and of dubious value. First, the laboratory techniques used for determining uric acid in biological fluids measured a whole complex of reducing substances, not uric acid alone.⁵ In addition, the origin of endogenous uric acid was unknown, resulting in inadequate dietary preparation of the patients. At the time of the studies of Stander and Cadden, 6, 7 it was believed (Scheme A, Fig. 1) that uric acid was a true end product of metabolism and that all of the urinary uric acid arose from either degradation of tissue nucleoprotein (endogenous uric acid) or from ingested foods of high purine content (exogenous uric acid). On this basis, limitation of ingested purine by means of a purine-free diet permitted the use of the urinary uric acid content as a measure of endogenous uric acid metabolism. Studies in laboratory animals and man, however, using isotope-labeled uric acid or its precursors, have led to a concept of uric acid metabolism that is much more complex (Scheme B, Fig. 1) and indicate that uric acid is neither a true end product nor does it arise solely from ingested purines. Our present concept differs from the previous one in several respects:

1. Several amino acids may be synthesized to uric acid. The purine fragments of nucleoproteins are built up, de novo, from these amino acids, formate,

^{*}This project has been supported, in part, by Grant No. A-252, from the Institute for Metabolic and Arthritic Diseases, U. S. Public Health Service.

and carbon dioxide, and eventually are oxidized to uric acid.⁸ Tissue nucleoprotein is not constructed from ingested purine but from purine molecules synthesized in the body. Therefore, any study of urate metabolism must include some control of ingested protein as well as ingested purine.

2. Uric acid is not invariably an end product of metabolism.⁹ While no enzyme capable of destroying uric acid has ever been demonstrated in the liver or any other human tissue, such an enzyme is present in intestinal bacteria. About 40 per cent of ingested urate is converted to urea and ammonia.¹⁰ The degree of conversion (uricolysis) of exogenous urate (40 per cent) is greater than that of endogenous urate (20 per cent). The conversion of intravenously administered uric acid to urea and ammonia, however, is not dependent on intestinal bacteria.¹¹ Uricolysis of parenterally administered urate occurs in the absence of bacterial enzyme activity, and the mechanism is unknown.

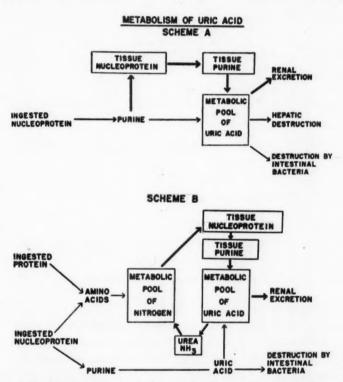


Fig. 1.-Uric acid metabolism in man. Scheme A, old concept, Scheme B, present concept.

In summary, the urinary excretion of uric acid in patients on a purine-free diet is a reflection of the rate of urate production, the rate of uricolysis, and renal function in respect to urate excretion. It is obvious, then, that no matter what the dietary control of the patient, the daily excretion of uric acid is merely the sum of these three factors operating simultaneously, and, therefore, the classical technique of limiting intake and measuring output cannot isolate and quantitate these separate functions.

TABLE I. URATE METABOLISM IN PREGNANT AND NONPREGNANT WOMEN AND PRE-ECLAMPTIC PATIENTS

CODE	WEEKS OF GESTATION	PLASMA URATE (MG. %)	N15 INJECTED (MG.)	MISCIBLE POOL (GM.)	TURNOVER RATE (POOLS/DAY)	TURNOVER NUMBER (GM./DAY)	URIC ACID (GM./DAY)	TURNOVER NUMBER— URINARY URIC ACID	% N15
Nonpregnant.	ant.	G	000	0	2				
K	1	20.00	3.96	0.53	0.76	0.41	0.40	0.01	92
ප	1	5.5	3.96	0.75	0.76	0.58	0.52	90.0	72
Normal Preg-	reg-								
nant.									
Ι	90	4.3	2.64	1.37	0.49	0.66	0.44	0.22	65
r	37	5.5	2.64	1.47	0.41	0.58	0.58	0000	65
K	33	3.8	3.71	1.27	0.47	0.59	0.62	-0.03	80
T	39	6.1	3.71	1.12	0.37	0.42	0.42	0.00	69
Pre-									
eclampsia	ia.								
A	34	8.7	2.66	2.62	0.26	0.69	0.26	0.43	26
0	38	6.3	3.96	1.45	0.50	0.73	0.36	0.37	37
田	40	5.7	3.96	1.69	0.39	99.0	0.37	0.29	47
5	35	5.3	3.96	1.73	0.53	0.95	0.50	0.45	40
M	29	0.6	3.71	2.27	0.45	1.02	0.47	0,55	40
Z	40	1	3.96	2.33	0.48	1.13	0.64	0.49	42
Д	335	6.2	3.96	1.56	0.62	0.97	0.67	0.30	59

This problem has been solved, in part, by the use of heavy nitrogen (N15) labeled uric acid. If uric acid is synthesized to contain N15, and this material is injected intravenously, the administered urate will mix with all or some portion of the urate within the body (Fig. 2). This quantity with which the injected material will mix is known as the miscible pool of urate. Theoretically, each day, new, unlabeled urate is produced and enters this pool. At the same time both labeled and unlabeled urate are leaving the pool as a result of either renal excretion or uricolysis. As a result of these metabolic phenomena, the concentration of labeled urate in the miscible pool becomes smaller and smaller. The rate at which the concentration of labeled urate declines is called the turnover rate and is expressed as the percentage of the pool exchanged per day. The mathematical product of the turnover rate and the miscible pool is the turnover number, or the quantity of urate in the pool that is replaced each day. If the miscible pool is of constant size, the turnover number is a measure of the rate of production of urate. The kidney presumably cannot differentiate between labeled and unlabeled uric acid, and therefore the concentration of

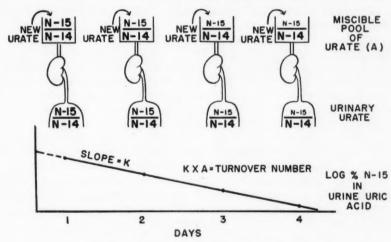


Fig. 2.—The turnover rate of uric acid.

labeled uric acid in the urinary uric acid is identical to the concentration of labeled material in the miscible pool. It is this concentration of labeled nitrogen in the urinary uric acid nitrogen that is determined by the mass spectrometer. If these concentrations of isotope in the urinary uric acid nitrogen are then plotted semilogarithmically against time, the concentration of isotope in the uric acid pool at the time of mixing may be estimated, and from this value the miscible pool calculated.

Methods and Materials

Uric acid was synthesized containing 7.50-8.07 atoms per cent excess of $N^{15, 12}$. Patients were prepared by consuming a low purine diet prior to and during the urine collection periods. Fish, meat, eggs, and other foods high in purine content were eliminated. The patient was permitted one glass of milk daily. Adequate caloric intake was maintained by the ingestion of vegetables of low purine content and fruits ad libitum. The isotope containing

urate was dissolved in a minimal quantity of alkali, diluted to 50 c.c. volume with 5 per cent glucose, and administered intravenously over a period of 10 to 20 minutes. Urine collections were obtained continuously for periods ranging from 10 to 24 hours for 5 days. Uric acid was extracted from urine, and its content of isotopic nitrogen determined on the mass spectrometer. Plasma and urinary uric acid concentrations were obtained by the enzymatic-spectrophotometric method of Kalckar as modified by Praetorius.

Results (Table I)

Two nonpregnant, 4 pregnant, and 7 pre-eclamptic patients were studied. The normal pregnant women were 33 to 39 weeks pregnant. The toxemic patients were all young primigravidas 29 to 40 weeks pregnant. The plasma urate concentrations in normal pregnant women vary from 3.8 to 6.1 mg. per cent. Only 2 of the toxemic patients were considered hyperuricemic. The miscible pool of uric acid in the normal pregnant women was surprisingly large (1.12 to 1.47 Gm.), and the miscible pool of the toxemic patients was even larger (1.45 to 2.62 Gm.). The quantity of urate replaced in the pool each day, the turnover number, is similar in both the pregnant and nonpregnant women, 0.41 to 0.52 Gm. and 0.42 to 0.62 Gm., respectively. In the toxemic patients, the turnover number ranged from 0.66 to 1.13 Gm. per day, indicating excessive urate production.

The quantity of urate produced and excreted is similar in pregnant and nonpregnant women. Only one patient, I, showed any significant difference in urate production and excretion. This value, however, is obtained by subtracting the quantity of urate in the urine, a chemical determination, from the turnover number, a result obtained solely from isotope analysis. Any contamination of the diet with purine nitrogen, and some was permitted in this study, would render this difference smaller than its true value. If, however, we use the isotope recovery value as a measure of the excretion of the urate produced, we find that the pregnant and nonpregnant women in this study excreted about 75 per cent of the injected material. In every case of toxemia in this study there was a considerable difference between urate produced and urate excreted. The percentage of N¹⁵ recovered in the urine was 26 to 59 per cent in the toxemic patients; 65 to 80 per cent in the normal pregnant women; and 72 and 76 per cent in the nonpregnant women.

Summary of Results (Table II)

1. The miscible pool of urate in pregnant women in the third trimester of pregnancy (1.12 to 1.47 Gm.) is twice as large as the miscible pool in non-pregnant women (0.53 to 0.75 Gm.) and similar in size to that of normal males (0.90 to 1.30 Gm.).

TABLE II. A COMPARISON OF URATE METABOLISM IN MEN AND PREGNANT AND NONPREGNANT WOMEN

	POOL (GM.)	TURNOVER RATE (POOLS/DAY)	TURNOVER NUMBER (GM./DAY)	INJECTED N ¹⁵ RECOVERED (PER CENT)
Normal males*	0.90-1.30	0.60-0.85	0.72-0.87	75-80
Nonpregnant females	0.53 - 0.75	0.76	0.41 - 0.58	72-76
Pregnant females	1.12-1.47	0.37 - 0.48	0.42 - 0.66	65-80
Pre-eclamptic patients	1.45-2.62	0.26 - 0.66	0.66 - 1.02	26-59

^{*}From Benedict, Forsham, and Stetten.9

^{2.} The turnover number of urate is similar in both normal pregnant (0.42 to 0.66 Gm.) and nonpregnant (0.41 to 0.58 Gm.) women. This is less than that of normal males.

10

0

g

ts

0-

d.

ic na

g. he

ly

as

ch

nt

li-

nd

ce

b-

he n-

nis

er.

ate

dy

nia nd

59

nt

ter

on-

nal

NT

ant

3. Comparison of urate production and excretion suggests that women, both pregnant and nonpregnant, excrete almost as much urate as is produced. Only about 65 to 80 per cent of the injected N¹⁵ is recovered, however, indicating that some degree of uricolysis occurs in women as well as in men.

4. Some patients with acute toxemia manifest increased pool size and increased turnover number.

5. All these patients with acute toxemia produce more urate than is excreted. Only 25 to 59 per cent of the N¹⁵ injected was recovered during the period of the study. This is in marked contrast to the normal pregnant and nonpregnant patients in whom 65 to 80 per cent was recovered.

Comment

The size of the miscible pool of urate is a reflection of the size of the active protoplasmic mass, the rate of ingestion of dietary purines or other uric acid precursors (e.g., glycine), the rate of oxidation of tissue purines, the rate of destruction of urate by intestinal bacteria, and the rate of urinary excretion. Increased loss of urate by means of more efficient excretion of uric acid or by increased destruction of urate by intestinal bacteria or any other means would result in a smaller pool. High protein or purine diets or excessive catabolism of tissue purines would tend to produce a larger pool. It is evident from the data that no gross deviation from normal in any of these rates is present in normal pregnancy. How, then, may the large size of the miscible pool of urate in normal pregnant women be explained?

During pregnancy, marked alterations in body composition occur. These changes are a gross increase in the lean body mass, far greater than that anticipated from the weight increment, and some loss of fat.¹⁵ The net result of these changes is such that the body of the pregnant woman contains active protoplasmic mass and storage fat in proportions usually identified with the normal male population. We believe that the increased pool of urate is merely a reflection of these alterations in body composition.

The accumulation of urate during pregnancy is of the order of 600 mg. If this material were accumulated over the first 210 days of gestation, it would represent an excess of urate entering the pool over urate leaving the pool of only 3 mg. per day, a quantity too small to be detected by the techniques available for the measurement of urate production or excretion.

While the size of the miscible pool of pregnant women approaches that of normal males, the turnover number is smaller and is the same as that found in nonpregnant women. Despite the fact that a considerable quantity of cellular material (nucleoprotein) is synthesized during pregnancy there is no evidence of increased urate production.

Patients with acute toxemia of pregnancy are characterized by a large miscible pool, and a large difference in the rates of urate production and urate excretion. In addition, in some of these patients, urate is overproduced. These data are interpreted to lend further support to the thesis that the hyper-uricemia found in some patients with acute toxemia is the result of the inability of the kidney to excrete uric acid properly. One of the major criticisms of this thesis is the fact that most mild cases of toxemia do not manifest hyperuricemia even though renal function tests in these same patients indi-

cate increased tubular reabsorption of urate with or without decreased glomerular filtration rates. The ability of patients with toxemia to get rid of urate through some mechanism other than renal excretion, presumably uricolysis, is responsible for the frequent occurrence of normal plasma urate concentrations in toxemic patients, whose rates of renal excretion of urate are decreased.

The significance of the increased rate of production of urate in some patients with acute toxemia is not determined by this study. It is known, however, that some women with pre-eclampsia are in relative negative nitrogen balance. This signifies that tissue is breaking down, and in clinical states of rapid tissue destruction, urate is overproduced. Increased rates of urate production in toxemic patients may signify protein catabolism. On the other hand, a second possible explanation is available. It has been demonstrated that some patients with gout convert amino acids to urate at an excessive rate.

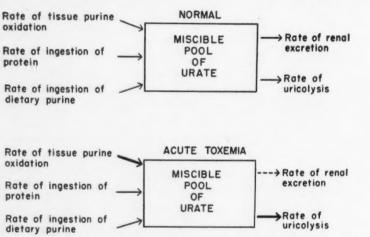


Fig. 3.—Changes in urate metabolism in normal pregnancy and in acute toxemia.

In fact, the rate of conversion is so rapid that it is doubtful that the normal pathway of synthesis of amino acid to purine and oxidation of purine to urate could occur. It has been suggested that this phenomenon in patients with gout represents the acquisition of a pathological metabolic system whereby amino acids are converted to urate by more direct means. Studies are in progress to determine whether or not such an abnormality of amino acid metabolism may be present in patients with pre-eclampsia.

It is obvious from the foregoing that the determination of the plasma urate concentration can hardly be of much clinical usefulness. The factors operative in the production of a particular level of plasma urate concentration in an individual patient are multiple (Fig. 3). The rate of destruction of urate, the rate of excretion of urate, the state of nitrogen metabolism, and the available volume of distribution of urate—all these factors are operative in every patient with toxemia, and the metabolic design is such that the plasma urate concentration tends to remain within normal limits. Conversely, even though the plasma urate level may be within normal limits in toxemic patients,

active destruction of urate is present and inadequate renal clearance can be demonstrated in most patients. These two pathophysiological processes offset each other, and only when the rate of urate production exceeds the rates of excretion and destruction does the plasma urate concentration rise.

The significance of these gross alterations in urate excretion and destruction are unknown. What factors are responsible for their occurrence? these phenomena of increased urate production and urate destruction injurious to the patient or fetus? These are the truly significant questions, and they are not answered by this study. Nonetheless, these alterations in urate metabolism stand among the few truly qualitative biochemical phenomena known to us today that differentiate the patient with acute toxemia from normal pregnant women.

Summary

Uric acid labeled with N¹⁵ was administered to 2 nonpregnant women, 4 pregnant, and 7 toxemic women. Normal pregnant women differ from nonpregnant women in that the uric acid pool is grossly enlarged. Urate production and loss occur at a similar rate in both, however.

Patients with acute toxemia manifest even larger urate pools and more rapid rates of production of urate than normal pregnant women. The most constant and significant aspect of urate metabolism in patients with preeclampsia is the marked increase in the rate of uricolysis.

Excessive renal tubular reabsorption of urate tends to produce elevated plasma urate concentrations. Excessive uricolysis tends to lower plasma urate These two phenomena offset each other, resulting in normal concentrations. plasma urate concentrations in most cases of acute toxemia.

I wish to thank Drs. Newlin F. Paxson, Thaddeus Montgomery, and Mary DeW. Pettit for the use of patients on their services at the Philadelphia General Hospital; Dr. M. John Boyd, Head of the Department of Biological Chemistry, Hahnemann Medical College, for his advice and encouragement; and Joy Seitchik and Anthony Szutka for their excellent technical assistance.

References

- 1. Dieckmann, William J.: The Toxemias of Pregnancy, ed. 2, St. Louis, 1952, The C. V. Mosby Company.
- 2. Seitchik, J.: Am. J. Obst. & Gynec. 65: 981, 1953.
- Chesley, L. C., and Williams, L. O.: Am. J. OBST. & GYNEC. 50: 367, 1945.
 Chesley, L. C.: M. Clin. North America, 35: 699, 1951.

- Chesley, L. C.: M. Clin. North America, 35: 699, 1951.
 Kalckar, H. M., and Shafran, M.: J. Biol. Chem. 167: 429, 1947.
 Stander, H. J., and Cadden, J. F.: Am. J. Obst. & Gynec. 28: 856, 1934.
 Cadden, J. F., and Stander, H. J.: Am. J. Obst. & Gynec. 37: 37, 1939.
 Buchanan, J. M., Sonne, J. C., and Delluva, A. M.: J. Biol. Chem. 173: 81, 1948.
 Benedict, J. D., Forsham, P. H., and Stetten, DeW., Jr.: J. Biol. Chem. 181: 183, 1949.
 Geren, W., Bendich, A., Bodansky, O., and Brown, G. B.: J. Biol. Chem. 183: 21, 1950.
 Wyngaarden, J. B., and Stetten, DeW., Jr.: J. Biol. Chem. 203: 9, 1953.
 Cavalieri, L. F., Blair, V. E., and Brown, G. B.: J. Am. Chem. Soc. 70: 1240, 1948.
 Rittenberg, D., Keston, A. S., Rosebury, F, and Schoenheimer, R.: J. Biol. Chem. 127: 291, 1939. 291, 1939.
- 14. Praetorius, E.: Scandinav. J. Clin. & Lab. Invest. 1: 222, 1949.
- Seitchik, J., and Alper, C.: S. Clin. North America 34: 1535, 1954.
 Mukherjee, C. L., and Govan, A. D.: J. Obst. & Gynaec. Brit. Emp. 58: 701, 1951.

FURTHER EXPERIENCE WITH APRESOLINE IN TOXEMIA AND HYPERTENSION OF PREGNANCY

HUMBERT L. RIVA, LIEUTENANT COLONEL, MC, USA, WOODROW L. PICKHARDT, LIEUTENANT COLONEL, MC, USA, ROBERT H. HOLZWORTH, CAPTAIN, MC, USA, AND ROBERT L. SHERMAN, MAJOR, MC, USA

(From the Obstetrical-Gynecological Service, Walter Reed Army Hospital, Washington, D. C.)

NE of the interesting new antihypertensive agents used in toxemia and hypertension of pregnancy is 1-hydrazinophthalazine (Apresoline) first studied by Gross, Druey, and Meier¹ in 1950. These Swiss investigators, working on animals, demonstrated that the phthalazine group of drugs act as vasodepressors, increasing the pulse rate and the renal blood flow. Other investigators²⁻⁶ found that the drug produced a hypotensive state as well as a vasodilatation of the kidney vascular bed, resulting in increased renal blood flow. McCall, and Hafkenschiel and co-workers studied cerebral blood flow after administration of Apresoline and reported a decreased cerebral vascular resistance, an increased cerebral blood flow, and oxygen utilization by the brain. Assali and Suyemoto, using a small series, concluded that after one intravenous dose of 1-hydrazinophthalazine the average reduction in blood pressure in toxemias of pregnancy was 26 per cent systolic and 43 per cent diastolic, with the diastolic responding first and to a greater degree. The average blood pressure reduction in the hypertensive group was 11 per cent systolic and 19 per cent diastolic.

As yet, the site of action of Apresoline is unknown, but Freis and Finnerty¹⁰ believe that there is strong evidence for vasodilatation by reduction in the outflow of sympathetic vasopressor impulses by central action. There is, however, a possibility of direct action of Apresoline on vessel walls.¹¹

There is a marked increase in cardiac output after Apresoline, according to Wilkinson, Backman, and Hecht.¹² The increase in renal blood flow is roughly proportional to the increase in cardiac output.⁶

Assali, Neme, and Rosenkrantz¹³ studied the hypotensive effects of a mixture of *Veratrum viride* alkaloids (Deravine) in combination with Apresoline in normal pregnancy, toxemia of pregnancy, and in essential hypertension associated with pregnancy. They concluded that the effect on the blood pressure of the two drugs mixed together was not more than the additional effect of each alone. Also, the bradyeardia characteristic of Veratrum, and the tachycardia peculiar to Apresoline cancelled each other. Consequently, the pulse rate remained practically unchanged when the two drugs were used together.

The results of 1-hydrazinophthalazine in 34 pregnant toxemic and hypertensive patients were studied by Sherman and Riva.¹⁴ Vasodepressor repsonse was achieved in all but one of the 29 patients who were given the drug intra-

venously. There was an unsatisfactory response with oral and subcutaneous administration of the drug in these patients. Intravenous Apresoline was used very effectively by Jordan¹⁵ in cases of pre-eclampsia and eclampsia. McCall¹⁶ used a combination of Apresoline and Unitensen on pregnant toxemia patients and discovered that this preparation eliminated some of the disagreeable effects of each substance. The pulse was affected less, cerebral functions were normal, and the adaptive reflexes were present. He stated that "there are fewer side effects, such as headache, vomiting, flushing of the skin, and restlessness," and also that 1-hydrazinophthalazine is the "only acceptable therapeutic hypotensive agent which does not interfere with kidney function,

Volume 72

8-

n-

n re

is

a soon es-

of

ıy-

lse

er.

er-

nse

ra-

Using a small series, Chapman, Strozier, and Magee¹⁷ found Apresoline to be a highly satisfactory drug for patients with hypertensive vascular disease, pre-eclampsia, and eclampsia. They found a significant drop in both the systolic and diastolic blood pressure. Dramatic clinical responses were noted also, with oral and intramuscular Apresoline, in about 50 per cent of the patients.

and that brings about renal vasodilatation and increase in the kidney flow."

Assali¹⁸ summarized the effects of the common hypotensive drugs, including the central-acting type, the ganglionic blocking agents, and the adrenergic blocking agents. He concluded that Veratrum and Apresoline "seem to be the most effective and the most indicated in the treatment of the acute phase of toxemia." These two drugs "produced the greatest fall in blood pressure; Apresoline alone increased renal plasma flow . . ." and decreased the total renal resistance.

Present Studies

Apresoline (1-hydrazinophthalazine) has now been evaluated as follows in 67 pregnant patients at Walter Reed Army Hospital, Obstetrical Service: 52 patients received the drug intravenously, 9 patients received the drug orally and intravenously, 6 patients received the drug orally or subcutaneously..

Classification.—Patients were divided into the following groups:

I.	Pre-eclampsia	34
II.	Hypertension of labor	19
III.	Hypertensive vascular disease	8
IV.	Hypertension with superimposed toxemia	3
V.	Eclampsia	2
VI.	Pre-eclampsia with chronic glomerulonephritis	1
	Total	67

A group of patients who manifested the hypertensive state for the first time when in labor have been classified by this institution as Group II. There was neither albuminuria nor edema, no history of hypertension, and blood pressures returned to normal in the puerperium. As has been mentioned, these patients have been classed as hypertensive at this institution. It is felt, however, that, rather than to classify them with inadequate data, a special group might be more accurate for diagnosis, pending the long-term follow-up which is necessary to establish a true diagnosis of hypertension.

Group VI includes only one patient who had a history of severe chronic glomerulonephritis with a superimposed pre-eclampsia, and it was felt this should be considered separately.

Mode of Administration.—Thirty-eight patients were given control therapy followed by the administration of the drug. An attempt was made to lower the blood pressure with two or more of the following drugs: 1 to 3 Gm. of intravenous or intramuscular magnesium sulfate, 200 to 500 mg. of Nembutal intravenously, 50 to 150 mg. of intravenous or intramuscular meperidine, 10 to 15 mg. of morphine sulfate, or 200 mg. of oral phenobarbital. If there was no response, or if the response was minimal, Apresoline was given. Those not in labor were given at least 24 hours of bed rest prior to the use of control therapy. Those already in labor were given several hours of control therapy prior to the administration of Apresoline.

Twenty-nine patients were given Apresoline intravenously without control therapy.

Intravenous Administration.—Intravenous injection was carried out in the following manner: Apresoline, 20 to 40 mg., was given slowly over a 5 to 10 minute period. Maximal responses could usually be demonstrated 10 to 20 minutes after initiation of the injection. Two physicians were always present, one taking blood pressures, the other administering the drug. The blood pressure was recorded at 10 to 20 second intervals during the injection and only as much of the drug was used as was necessary to reduce the pressure to within normal limits with the emphasis placed on the diastolic pressure. astolic always fell first and to the greater degree. In fact, on occasions, the systolic pressure increased over the control, but then fell at least to control level and more often lower, as the actual percentile reductions listed verify. Blood pressures were recorded at 5 minute intervals following completion of the injection of a half hour period, then every 15 minutes for the next half Thirty minute intervals, or more frequently if necessary, were then observed between pressure recordings. The pulse rate and the time of the onset of facial flush were also noted. This routine was again followed if another dose was indicated.

Results

Since the chief response to the Apresoline therapy is a drop in blood pressure and a rise in pulse rate, these two results were recorded. The mean blood pressure response was then plotted in each category (Figs. 1 to 6).

The maximal blood pressure response was usually found within 45 to 60 minutes after the injection of the drug. The average duration of action was 1 to 6 hours. The dosage varied between 20 and 40 mg. of Apresoline in order to get a good response. It was found, however, that the optimum dose for the average patient was 40 mg. intravenously. Some patients received multiple doses of Apresoline.

The blood pressure reduction, by groups, is shown in Table I.

The average maximum increase in pulse rate following Apresoline was recorded within 30 to 45 minutes as follows:

- I. Pre-eclampsia, 36.2 beats per minute increase.
- II. Hypertension of labor, 8.0 beats per minute increase.
- III. Hypertensive vascular disease, 8.0 beats per minute increase.
- IV. Hypertension with superimposed pre-eclampsia, 22.6 beats per minute increase.
 - V. Eclampsia (and eclampsia superimposed on hypertensive vascular disease), 22.0 beats per minute increase.

TABLE I. MEAN REDUCTION IN BLOOD PRESSURE WITH APRESOLINE

					MIN	UTES			
		1	.5	3	0	4	5	6	0
		SYS-	DIAS-	SYS-	DIAS-	SYS-	DIAS-	SYS-	DIAS-
		TOLIC (MM.	TOLIC						
	GROUP	Hg)	Hg)						
Group I	Pre-eclampsia (Fig. 1)	20.1	25.9	30.4	32.9	34.9	36.3	_	-
Group II	Hypertension of labor (Fig. 2)	19.0	33.0	23.6	41.0	15.0	38.0	20.0	32.5
Group III	Hypertensive vascular disease (Fig. 3)	18.5	31.5	23.5	31.0	30.5	45.0	35.0	45.0
Group IV	Hypertension with superim- posed pre-eclampsia (Fig. 4)	3.8	16.0	8.7	19.8	12.0	23.0	15.0	22.0
Group V	Eclampsia and eclampsia superimposed on hyper- tensive vascular disease (Fig. 5)	24.0	11.6	37.0	15.3	40.0	15.0	33.0	27.0
Group VI	Pre-eclampsia with chronic glomeronephritis (Fig. 6)	15.0	10.0	35.0	25.0	50.0	40.0	46.0	40.0

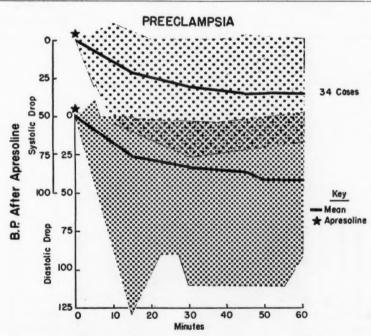


Fig. 1.—Shows decrease in blood pressure in pre-eclampsia caused by Apresoline.

Since there was an insufficient number of recorded cases in II and III above, to be significant, and taking an average of Groups I, IV, and V, the mean is 26.9 beats per minute increase.

Oral and Subcutaneous Administration of Apresoline.—Fifteen patients received 1-hydrazinophthalazine orally, but 9 of these also received the drug intravenously, thereby clouding the picture somewhat. Six patients received the drug purely by the oral or subcutaneous routes.

The dosage varied up to 160 mg. subcutaneously, and up to 400 mg. orally per day. Although the results varied, 2 pre-eclamptic patients had a fairly

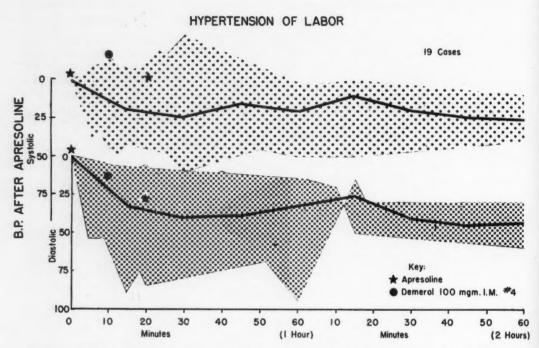


Fig. 2.—Depicts effect of Apresoline and Demerol on hypertension associated with labor.

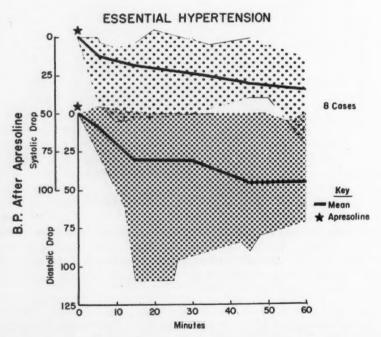


Fig. 3.—Illustrates drop in blood pressure produced by Apresoline in pregnant patients with essential hypertension.

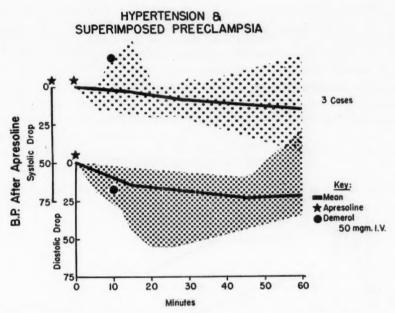
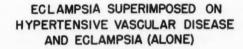


Fig. 4.—Shows smaller drop in blood pressure produced by Apresoline.



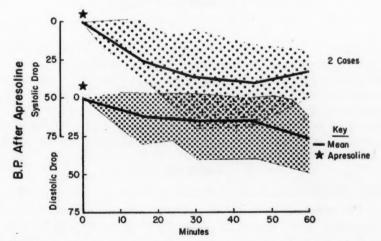


Fig. 5.—Depicts effect of Apresoline on blood pressure in 2 patients with convulsions.

good sustained hypotensive response, and one pre-eclamptic patient had a good response when the oral dosage was raised to 200 mg. a day. It apears that occasionally this type of therapy may have a place for the patient not in labor.

Side Effects.—The characteristic signs which indicated a good patient response to the drug included facial flush, tachycardia, and a bounding pulse. These were noted in all patients who received the drug intravenously. These symptoms occurred from 5 to 10 minutes after the injection of the drug was begun and usually disappeared within 30 minutes.

Pulsating or throbbing headaches were rarely noted, but this symptom when present was not incapacitating and did not require any further therapy. No other untoward symptoms were noted in the series.

PREECLAMPSIA & CHRONIC GLOMERULONEPHRITIS

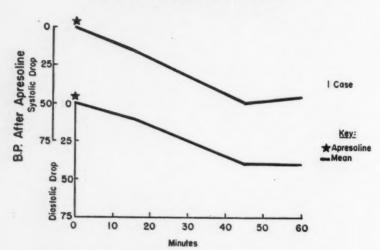


Fig. 6.—Shows marked effect produced by Apresoline.

In the series of 67 cases, there were 5 stillborn infants and 2 neonatal deaths of premature infants or immature infants. The incidence of premature infants was high in this series, but many of these survived. As was mentioned by Sherman and Riva, 14 a reduction in blood pressure should tend to prevent death due to cerebral hemorrhage and edema coincident with toxemia. Some of the stillborn infants showed placental infarction and premature separation of the placenta. The fetal heart tones were unaffected by Apresoline.

Comment

Two cases of eclampsia have been treated since the preliminary report was submitted. The mean drop in blood pressure was significant and the systolic pressure responded much better than the diastolic. The duration of response was good in both cases, the blood pressure being maintained at the lower levels for several hours at a time. One patient was given Apresoline intermittently for 18 days without untoward effects.

There was no noticeable change in the patients' daily intake and output. The 24 hour albumin studies showed no demonstrable effect. And again, for

the second series, there was no evidence of circulatory embarrassment. The pulse remained bounding and of good quality even at low hypotensive levels.

Summary

- 1. Results of 1-hydrazinophthalazine (Apresoline) therapy in 67 pregnant toxemic and hypertensive patients have been presented.
- 2. The mean vasodepressor response was significant in all six groups of patients, and less marked in the patients with a previous history of hypertension.
- 3. The average tachycardia after Apresoline was noted within 30 minutes, and amounted to an increase of about 20 to 30 mm. Hg.
- 4. The infant mortality, amounting to about 7 per cent, was not attributed to the use of Apresoline.
- 5. Oral or subcutaneous use of Apresoline may have a place in a few selected nonacute cases.
- 6. Apresoline is highly recommended for the control of the hypertensive aspects of pre-eclampsia and hypertension in pregnancy.

Addendum.—Twenty additional cases have been treated with Apresoline since the above publication, and the results are comparable. The intravenous drip method of administering Apresoline has been found to be more efficacious in maintaining a desired lowering of blood pressure, thus avoiding a precipitous drop in blood pressure, which might well result in placental shock and fetal hypoxia.

References

- Gross, F., Druey, J., and Meier, R.: Experientia 6: 19, 1950.
 Grimson, K. S., and Chittum, J. R.: Am. J. Med. 7: 251, 1949.
 Craver, B. N., and Yonkman, J. F.: Federation Proc. 9: 265, 1950.
 Reubi, F. C.: Helvet med. acta 16: 297, 1949.
 Reubi, F. C.: Proc. Soc. Exper. Biol. & Med. 73: 102, 1950.
 Med. 73: 102, 1950.

- Moyer, J. H., Handley, C. A., and Huggins, R. A.: J. Pharmacol. & Exper. Therap. 103: 368, 1951.
- McCall, M. L.: Am. J. Obst. & Gynec. 66: 1015, 1953.
 Hafkenschiel, J. H., Friedland, C. K., Yobaggy, J., and Jeffers, W. A.: Am. J. Med. 14: 509, 1953.

- 14: 509, 1953.

 9. Assali, N. S., and Suyemoto, R.: Am. J. Obst. & Gynec. 64: 1021, 1952.

 10. Freis, E. D., and Finnerty, F. A., Jr.: Proc. Soc. Exper. Biol. & Med. 75: 23, 1950.

 11. Stunkard, A., Wertheimer, L., and Redisch, W.: J. Clin. Invest. 33: 1047, 1954.

 12. Wilkinson, E. L., Backman, H., and Hecht, H. H.: Am. J. Med. 13: 101, 1952.

 13. Assali, N. S., Neme, B., and Rosenkrantz, J. G.: Obst. & Gynec. 3: 270, 1954.

 14. Sherman, R. L., and Riva, H. L.: Am. J. Obst. & Gynec. 67: 1074, 1954.

 15. Jordan, W. K.: Am. J. Obst. & Gynec. 68: 618, 1954.

 16. McCall, M. L.: Obst. & Gynec. 4: 403, 1954.

 17. Chapman, E. R.. Strozier, W. E., nad Magee, R. A.: Am. J. Obst. & Gynec. 68: 1109. 17. Chapman, E. R., Strozier, W. E., nad Magee, R. A.: Am. J. Obst. & Gynec. 68: 1109,
- 18. Assali, N. S.: Obst. & Gynec. Surv. 9: 776, 1954.

RETENTION CATHETER FOLLOWING VAGINAL DELIVERY

J. KENNETH PATTERSON, M.D., SANTA BARBARA, CALIF.

(From the St. Francis Hospital)

FOR many years, it has been the practice of most surgeons to place an indwelling retention catheter in the bladder of patients following the performance of pelvic surgery.¹ A recent article² reaffirms its value. A survey of the literature, however, fails to disclose previous routine use of the procedure following vaginal delivery.

During vaginal delivery the neck of the bladder or the urethra may sustain minimal-to-severe bruising or damage. Catheterized specimens taken during the first twenty-four hours are at times blood tinged. This is particularly true after difficult deliveries, whether owing to a large baby, malposition, or constricted pelvic outlet.

Apparently for this cause and perhaps also because of the use of sedation in labor, with unconscious undetected overdistention of the postpartum bladder, certain patients require postpartum eatheterization. In the control series in this study, 10 per cent of patients required catheterization for diagnosis or relief of retention despite the usual nursing aids such as ambulation, pouring water over the vulva, etc. Patients also should be considered who were finally able to void with these nursing measures after some interval of discomfort, or who were rendered uncomfortable from delay in bedpan service. (These latter can be very bitter in their complaints!)

"Early rising definitely decreases the need for catheterization following delivery." It has not eradicated the problem. Moreover, after an exhausting labor or when hemorrhage is to be feared or controlled, or after considerable sedation, very early ambulation is undesirable. During these early hours the bladder may become overdistended from absorbed body fluids even with little or no intake by mouth. It is also at times disconcerting to visit a patient in the hospital for a necessary postpartum examination only to find her on the first day interminably detained in the bathroom in an effort to empty the bladder.

It was found that the most stubborn of these cases often responded to the use of an indwelling eatheter, allowing the bladder complete rest for a twenty-four hour period or more. In the fall of 1953, therefore, I began to experiment with the use of a retention catheter inserted at the time of delivery in cases where trouble might be anticipated. Several types of catheter were tried: the straight catheter, which fell out too often; the Foley catheter, the use of which was time consuming and which at times leaked; an ordinary rubber mushroom catheter which was found quite satisfactory.

Method

This mushroom catheter (size No. 14) was inserted with a curved hemostat following stripping of the cord, delivery of the placenta, and repair of the episiotomy. A special director was found unnecessary. The catheter was taped with some slack up over the mons pubis in the midline, using two 1 by 5 inch strips of adhesive, one strip applied transversely across the shaved mons and one about 2 inches higher. These were covered by the perineal pad and belt. The catheter was then connected to a bottle on that side of the bed least exposed to visitors. It was found that taping the catheter in his way, rather than to the thigh, had these advantages: (1) the adhesive strips did not become soiled with lochial discharges, (2) the tubing did not become compressed under the patient, (3) free movement of the patient's legs was not impeded, and (4) the catheter was less likely to become dislodged.

Antibiotics were not given as a routine.

The catheter was allowed to drain freely until 8:00 A.M. the second morning after delivery. The patient remained in bed during this time (about thirty-seven hours on the average) although encouraged to move about in bed freely. On this second morning she was given a routine enema, the catheter was removed, and she was allowed up to the bathroom to expel the enema and for further bathroom privileges. Reasonably early ambulation was thus effected after at least twenty-four hours of controlled observation.

Results

The results of this partial experiment appeared satisfactory. There had been no complaints from patients, and of course none from the nurses, whose postpartum duties were simplified. It was therefore decided to insert a retention catheter as a routine for all the first 100 consecutive patients I delivered vaginally in my practice at the St. Francis Hospital, Santa Barbara, in 1954, beginning with January 1. Records of these 100 cases are summarized below. Used as a control were the first 100 consecutive vaginal deliveries in the same hospital by other operators in 1954 but cared for by the same nursing staff. Ten per cent of this control series required catheterization.

Summary of Data in the Retention Catheter Series .-

A careful analysis of these 100 consecutive cases in which a retention catheter was used post partum shows them to be a representative sample of the usual obstetrical practice. Thus the ages ranged from one patient of 16 years to two of 39 years. Gravidity ranged from 26 primigravidas to one gravida ix. Twenty-four had spontaneous deliveries, 68 low or outlet forceps, one midforceps, 7 were delivered by breech extraction (one set of twins), one by scalp traction for a stillborn infant. Episiotomy was performed on nearly all patients. There were no third-degree lacerations and no precipitate deliveries. Spontaneous labor occurred in 56 cases; labor was induced or semi-induced in 44 cases. The length of labor ranged from one to thirty hours, averaging seven hours. Babies weighed an average of 7 pounds, 8 ounces, ranging from 4 pounds, 4 ounces, to 10 pounds, ½ ounce, except for one stillborn premature weighing 1 pound, 13 ounces. There was one neonatal death due to multiple congenital anomalies (meningocele, etc.) and 2 stillbirths (one due to premature separation and one to torsion of the The usual sedation was a combination of Demerol, scopolamine, and magnesium sulfate, often with Trilene and followed by gas-oxygen-ether for delivery. At times pudendal block was used or intravenous Pentothal sodium after the baby was born. The shortest hospital stay was three days; the average was seven days. The incidence of cesarean section during this period was 4 per Two patients were delivered vaginally who had had previous cesarean delivery. There were 4 cases of antepartum bleeding from marginal placenta previa or separation and 3 cases of moderate toxemia requiring antepartum treatment.

There was no maternal death among these patients, no morbidity from any cause according to the temperature charts, and no symptoms of cystitis.

Table I summarizes the experience with urinary output.

TABLE I. URINARY OUTPUT IN PATIENTS WITH CATHETER DRAINAGE

	CATHETER	CATHETER DRAINAGE		VOIDED AFTER
	IN PLACE	ACTUAL	PER 24 HOURS	REMOVAL
Minimum	244 hours	1.750 c.c.	1.104 c.c.	
Maximum	56 hours	9,950 c.c.	5,760 c.c.	
Average	37 hours		2,355 c.c.	500 c.c. in 5 hour

There was no consistent reason found for the wide variation in urinary output and it seemed to bear little relation to fluid intake. This latter could not be accurately measured in these private patients, but usually the output exceeded the apparent intake. No sugar was found in the urine of those with large urinary output. The output of the mild toxemias of this series did not vary from the average appreciably. Since the output appears unpredictable in the first twenty-four hours, it is not surprising that some patients' bladders will become overdistended in a relatively short time following delivery.

One patient in this series required further catheterization after removal of the catheter, which had been in place for thirty-seven hours and had drained 2,300 c.c. She was a 31-year-old gravida i who had the largest baby in this series, 10 pounds, ½ ounce, delivered with some difficulty after a forceps rotation from posterior position. In her case the catheter had to be reinserted for twenty-four hours to control persisting urinary residual. It is possible that the initial catheter should have been retained in place longer in view of her difficult delivery.

Advantages of Use of the Retention Catheter .-

The nursing care of these patients was greatly simplified. Bedpans were no longer used in any postpartum case. Observation of the contraction of the fundus was more accurate during the early critical hours, since the overlying bladder was not at any time distended.

Although the patient was told that the catheter would be removed at any time she desired, it was found universally acceptable. Such unsolicited remarks as "it is a wonderful idea" were found common and gratifying. attitude was surprising since it had been expected that some of the more fastidious might object. Two factors had not been considered, however. First, it appears that some patients following delivery fear "an accident in bed" (to quote) from the bladder. There is a feeling of uncertainty in the pelvis due to the contracting uterus, the distended bladder, and a feeling of lack of bladder control. Knowing that the bladder is being kept empty gives these patients peace of mind. Second, the catheter does not seem to cause the local discomfort after vaginal delivery that commonly occurs after pelvic surgery or cesarean section. This may be due to the numbing effect of the pressure of the baby's head on the urethra at birth. This was also a surprise, since it had been considered that failure to void was due to spasm of the sphincter mechanism from reflex pain. This idea was held despite the fact that in our hands the use of Nupercaine ointment as a lubricant for the occasionally used catheter previously had proved not beneficial.

Although not subject to proof in this short series, postpartum bleeding seemed to be less on the average. This was my impression and that of the obstetrical nurses. It seems reasonable, however, on two counts. First, the fundus is more easily observed and massaged in the absence of an overlying distended bladder. Second, there may be a reflex action from the bladder which, when contracted, encourages a like contraction of the uterus. The relationship between bladder and uterine innervation has been noted elsewhere.4 There was no case of postpartum hemorrhage in this series. There was no cervical laceration in the series requiring suturing; the interior of the uterus was routinely explored with sponge forceps after delivery for retained secundines. All but 3 mothers of full-term normal babies nursed during their hospital stay.

Since the conclusion of the study, I have adopted the use of a retention catheter as a routine following all vaginal deliveries at both the St. Francis and the Cottage Hospital, Santa Barbara. The total so treated by the time this summary was completed was well over 200 cases. The single case previously noted was the only one which required further catheterization, and no complication due to the catheter has arisen in any case.

Conclusions

In this series of 100 typical and consecutive vaginal deliveries, followed by the routine use of an indwelling catheter according to the method described, the following facts were noted:

- 1. There was no morbidity in this series, nor any case of bladder irritation or infection.
- 2. The retention catheter eliminated the need for postpartum bedpans, yet early ambulation (in thirty-seven hours on the average) was maintained.
 - 3. The fundus was readily available for observation and massage.
- 4. The incidence of catheterization for further urinary retention after removal of the catheter was 0.5 per cent (one case in the larger series of over 200).
 - 5. Postpartum bleeding appeared less than usual.
- 6. The procedure added to the patients' comfort and was universally acceptable for both physical and psychological reasons.

References

- Kennedy, William T.: Am. J. Obst. & Gynec. 46: 506, 1946.
 Bomzee, Edward J.: West. J. Surg. 62: 325, 1854.
 Greenhill, J. P.: The 1947 Year Book of Obstetrics and Gynecology, Chicago, 1947, The Year Book Publishers, Inc., p. 213.
- 4. Theobald, G. W.: J. Obst. & Gynaec. Brit. Emp. 58: 763, 1951.

MATERNAL FACTORS IN PREMATURITY*

CLAIR E. FOLSOME, M.D., MARTIN L. STONE, M.D., LEONARD HIRSCH, M.D., AND BURTON KRUMHOLZ, M.D., NEW YORK, N. Y.

(From the Department of Obstetrics and Gynecology, New York Medical College and the Divisions of Obstetrics and Gynecology of the Metropolitan and Flower and Fifth Avenue Hospitals)

FORTY years ago our primary obstetric problem was a high maternal mortality rate. The problem of prematurity was relegated to the pediatrician. With the marked reduction in rates of maternal mortality, there has been a revival of interest in the causes of prematurity. Eastman,¹ Hellman,² Guttmacher,³ C. Randall,⁴ Potter,⁵ Kramer,⁶ Lund,² and Hughes⁵ have led this renaissance and impressed us all with the significance of "fetal salvage." The core of most fetal salvage programs in most prenatal clinics consists largely of greatly improved antepartum care. This topic now is truly in its reformation period.

With this concept in mind, we have reviewed the cases of premature birth at the Metropolitan Hospital and on the ward service at Flower and Fifth Avenue Hospitals to seek rewarding and potential leads for further studies on these problems. Among 2,400 recent deliveries we found a total of 380 premature births, an incidence of 6.3 per cent. Shapiro and Unger⁹ observed that of all the children born during the first 3 months of 1950, the latest interim with fully completed figures of the U.S. registration area, 7.4 per cent weighed 2,500 grams or less. In this national study, approximately two-thirds of these infants died in the neonatal period. The birth records for 1950, in most of the states, requested gestation age by the phrase "length of pregnancy in weeks" on the birth certificate. These authors reported that "many infants who would be considered premature according to gestation age weighed over 2,500 grams, and, conversely many of the low weight infants were reported as born at or near full term."

When classified according to the double criteria of prematurity, i.e., a birth weight of 2,500 grams or less and a gestation of 37 weeks or less, only 3 per cent of all liveborn infants appear to meet this dual definition of prematurity. In our clinical survey we accept the definition of prematurity as proposed by the American Academy of Pediatrics, as cited by Toback, 10, 11 "A premature infant is one who weighs 2,500 grams at birth regardless of the period of gestation." Further, we excluded all immature infants that weighed less than 1,000 grams at birth.

^{*}Presented at a meeting of the Section on Obstetrics and Gynecology, New York Academy of Medicine, April 26, 1955.

We find we can assign a definite maternal factor as related to prematurity in but 124 cases, or approximately 32 per cent of the series (Table I). Conversely, no specific maternal factor could be demonstrated in 252 instances, or in 67 per cent of this study series.

TABLE I. MATERNAL FACTORS IN PREMATURE LABOR

	NO. OF CASES	PER CENT
Toxemia of pregnancy	49	12.8
Plural births	38	10
Antepartum hemorrhage	12	3.1
Elective cesarean section	9	2.4
Medical and gynecological complications	16	3.2
	124	32.6
No maternal factor found	252	67.4
Total	380	100.0

Correlation of Age and Parity With Premature Labor.—There were 244 multiparous and 136 primiparous patients in this survey. Eighty-one, or 33.2 per cent, of the multiparous women gave a definite history of prior premature delivery. It is worth observing that 50 of the 136 primiparous patients, 37.7 per cent, were under the age of 20 years. Hacker and his associates observed premature births in 83 of their adolescent patients under 17 years of age, or a 17 per cent incidence of prematurity as compared to 13.5 per cent in all clinic cases. They considered early maternal age a factor in prematurity. They also observed that "many of these young patients have improper psychological preparation for pregnancy and are terrified of labor and delivery." Morrison observed that 15 per cent of 577 patients under the age of 15 delivered premature infants. Marchetti and Menaker observed an incidence of 12.0 per cent premature labors in the young obstetric patient.

Correlation of Prenatal Care to Prenature Labor.—Perhaps more cogent than psychological preparation is lack of proper antenatal care. Eighty-nine cases, 23.4 per cent, were accepted for delivery as "nonclinic" cases without prior prenatal care. Hacker and his co-workers observed that 49 per cent of their series had no antenatal care. Thus 1 of every 2 of Hacker's cases and 1 of every 4 of our series failed to report for any prenatal care. It is difficult to emphasize this point enough!

The specific maternal factors related to prematurity likewise could have received far greater control in our prenatal "problem clinics" to prevent prematurity had these patients reported early in pregnancy.

Toxemia of Pregnancy.—We found toxemia of pregnancy to be the most significant individual maternal factor, with 49 cases, or 12.8 per cent, a figure approximately 5 per cent higher than our clinic average of 7.0 per cent. Bookstover¹⁵ in his survey of 582 consecutive premature births observed toxemia in 78 cases, 13.4 per cent, or three times the incidence in general maternity admissions at the Norwegian Hospital in Brooklyn. Prompt preventive therapy directed to toxemia would greatly aid in the reduction of this maternal factor in producing premature labor.

Plural Births.—The second most frequent specific maternal factor associated with prematurity was plural births, 38 cases, or 10 per cent. In 9 of these 38 twin pregnancies there was an associated pre-eclampsia. Bookstover¹⁵ noted multiple births as an obstetric factor in 72 instances, or 12.3 per cent of his series of premature births. We agree with Bookstover that infants of inadequate weights, born in multiple pregnancies, are less an obstetric prob-

lem, since some of these low-weight infants are, in effect, truly more mature and have a greater chance of survival than infants of the same weight born singly. Special antepartum care is needed in multiple pregnancy, however. Plural pregnancy should be diagnosed as early as possible. Salt and activity should be sharply restricted. Patients should be advised to increase their rest periods and to abstain from travel and careless coition. The constant purpose is to increase the duration of gestation.

Antepartum Hemorrhage.—A third maternal complication which shows causal relationship to the onset of premature labor is antepartum hemorrhage. There were 12 cases of bleeding, or 3.1 per cent; 7 cases, or 1.8 per cent, from abruptio placentae, and 5 cases, or 1.3 per cent, from placenta previa. Bookstover¹⁵ reported 46 cases, or an incidence of 7.8 per cent, of antepartum hemorrhagic maternal complications in his series. The establishment of newer concepts of conservative management of placenta previa and abruptio placentae, often seen accompanying toxemia, now permits the obstetrician to indulge in a safer "intelligent procrastination" leading to the salvage of many infants heretofore lost.

Elective Cesarean Section.—A fourth complication contributing to premature delivery is elective repeat cesarean section, 9 cases, or 2.4 per cent, in our series. It is obvious that the older concept of "once a section always a section" has a corollary in the increase in the delivery of unsuspected premature infants. The determination of fetal size prior to actual delivery is at present uniquely difficult and, as we all know, frequently in error. Since this factor is a controllable and preventable element, until we have a more objective determination of fetal size, other than "experienced judgment," it is more judicious, we believe, to avoid delivery of an unsuspected small baby by allowing the initiation of true labor, as observed on the antepartum ward, prior to proceeding with the actual repeat section. Only 10 per cent of premature labors and deliveries are the result of the obstetrician's decision to terminate pregnancy upon maternal indications while over 90 per cent of premature labors occur spontaneously with or without a specific maternal cause. Shapiro and Unger,9 however, do report that there is an additional factor of physician responsibility other than time for elective repeat section. They note that among 63,925 live births in the first 3 months of 1950 there were 3,775 premature infants born while the doctor was not in the hospital. It must then be concluded that herein is an expression of "telephone obstetrics" with reassigned responsibility to less skilled attendants. In this study there occurred 662 neonatal deaths of these premature infants, 12.2 per cent of the 3,775 premature births.

Miscellaneous Medical and Gynecologic Complications.—Medical and gynecologic complications of pregnancy occurred in 16 of our cases, a combined incidence of 3.2 per cent: untreated syphilis, 9 cases, 2.4 per cent; rheumatic heart disease, 5 cases, 1.3 per cent; kidney disease, 1 case, 0.25 per cent; and fibroids, 1 case, 0.25 per cent. Taylor and his co-workers¹⁶ stressed the observation that when medical and surgical maternal complications are present there is a four- to fivefold increase in the incidence of prematurity.

Proper and active specific medical therapy following early diagnosis and recognition of the disease has reduced complications and early antepartum care can markedly lessen the frequency of prematurity associated with these medical disorders. To accomplish this, however, it is essential that we educate patients much more intensely to report earlier in pregnancy at the prenatal clinics.

The most outstanding finding we made was similar to that reported elsewhere, that in 252 instances, or 67.4 per cent, of the series we could determine

no maternal factor contributing to prematurity. It must be recalled that our cases are exclusively ward service cases of a low socioeconomic level and that in about 1 in each 4 of these cases the patient never appeared at a prenatal clinic. The patients are largely Puerto Ricans or non-white. While our facilities and staff are excellent we constantly face an attitude of indifference despite vigorous efforts to promote prenatal care.

We made no attempt to evaluate the intrapartum factors that would contribute to prematurity in our study. Bookstover¹⁵ emphasized this aspect considerably by stressing that 40.4 per cent of his series had received analgesics while 33.6 per cent had received more than light obstetric anesthesia.

Wallace and her group¹⁷ conducted a pilot study for one month in Brooklyn and concluded that there is need for increased prenatal standards and intrapartum programs directed toward salvage of premature infants.

Possible Dietary Factors.—Eastman¹⁸ has postulated that the majority of premature labors may be due to a dietary deficiency. Smith and her coworkers19 reviewed the food practices of obstetric patients in four North Carolina counties. This group advocated strongly that there be specific dietary regimes to meet the nutritional needs of pregnancy. They found principally a relatively low intake of foods that were good sources of protein, and a high carbohydrate intake. The Vanderbilt Cooperative Study of Maternal and Infant Nutrition²⁰ had 123 liveborn premature infants, and 16 stillborn premature infants in their series. The authors as yet, however, cannot establish a cause-and-effect relationship between maternal malnutrition and prematurity. Their next publication will be concerned with these aspects in greater detail. We concur with Tompkins21 that improvement in maternal nutrition effects a marked lowering in the incidence of premature labor in the series of patients in whom we could find no specific maternal cause. We observed but did not specifically calculate that approximately half of our patients were excessively overweight or underweight. Tompkins found an incidence of premature labor in 7.5 per cent of his patients who were 20 per cent overweight and a 22.2 per cent incidence in his patients who were 20 per cent underweight. These factors we are evaluating in an additional study.

Possible Emotional Factors.—A high percentage of our patients are extremely emotional at the time of delivery. While we have no yardstick to evaluate the possible relationship of the "fear-tension" or general adaptation syndromes to the onset of premature labor, we strongly suspect the presence of some psychosomatic factors in the induction of premature labor. It is our belief that a small percentage of patients escape the positive and negative polarity of the psychic ambivalence seen in early pregnancy wherein the patient vacillates from "I am glad I'm pregnant" to "I wish I had not become pregnant," and actually escapes spontaneous or induced abortion finally to arrive at a maladjusted psyche between the twenty-eighth and the thirty-seventh weeks. Then by some pharmacobiologic phenomenon not understood the patient enters premature labor. Ferguson²² was unable to induce labor, however, with therapeutic dose of ACTH. This hypothesis of psychosomatic influence warrants further investigation.

Recently in our clinic we have employed a new product, Releasin,* a potent and purified uterine relaxing factor obtained from the sow ovary, in the attempt to halt premature labor. Twenty milligrams of this purified extract are available in each cubic centimeter of the product. We have used doses of 60 to 600 mg. or 3 to 30 c.c. of Releasin. Abramson and Reid²³ have also reported the use of relaxin in the treatment of premature labor. In our

^{*}Chilcott-Warner Company.

early trials we have been able to halt premature labor successfully in 6 of 8 cases. In one case we postponed delivery for one month, allowing the infant to reach a weight of 3,030 grams. In our continuing study we will use the uterine receptor method of Karlson²⁴ to ascertain, if possible, the mechanism and effect of this new agent on uterine motility and the speed of cervical dilatation and effacement. To date we have observed no serious toxic effects of Releasin in dosages up to 600 mg., or 30 c.c., intramuscularly. Furthermore, we have also been able to halt true labor at full term in 6 other cases with premature rupture of the membranes.

What more can we do? We must continue intelligent individual studies. Bundeson²⁵ advocates the inculcation of an "alerter system" in approaching the problem of improving care for mothers and newborn infants in hospitals. In this system the individual physician is immediately "alerted" to possible preventable factors. Obviously these alerters are actually epidemiologically minded physicians participating in improved prenatal programs. As a corollary to this there must be present a well-organized intrapartum program designed to halt premature labor wherever feasible. Bundeson observed that such a system in one hospital was able to reduce the death rate in premature infants from a previous high in 1953 of 189.0 to a low in 1954 of 105.2 per 1,000 live births, or a 44 per cent drop; and from a rate of 9.6 in 1953 to 3.6 in 1954 for full-term babies.

Conclusions

A discussion based upon the evaluation of maternal factors in premature labor and premature birth is offered. In this series there were 2,400 deliveries, among which were 380 premature births, an incidence of 6.3 per cent. We could demonstrate possible maternal factors in but 1 of each 3 cases and no obvious maternal factors in 2 of each 3 cases. In addition to the usual complications of obstetrics we did observe that additional factors such as adolescence, obesity or underweight, and possibly certain psychosomatic factors in the mother were present. There was also an occasional delegation of responsibility by the physician.

We further have recently employed Releasin, a purified uterine relaxing factor, in an empirical clinical study. To date we have successfully halted premature labors in 6 of 8 cases, 75 per cent. These studies are continuing.

The answer to preventing prematurity rests in improved prenatal care and more efficient intrapartum organization, but primarily it rests upon the individual physician himself to individualize his cases. We urge further that all hospitals consider favorably the recent recommendations present in Bundeson's new "alerter system."

References

- 1. Eastman, N. J.: Williams Obstetrics, ed. 10, New York, 1950, Appleton-Century-Crofts,
- Lastman, N. J.: Williams Obstetrics, ed. 10, New Tork, 1990, Appleton-Century-Croits, Inc., p. 1000.
 Hellman, L. M.: Proceedings of Special Committee on Infant Mortality, County of New York, Evansville, Indiana, 1950-1951, published by Mead Johnson & Co., p. 1.
 Guttmacher, A. F.: New York M. J. 53: 2781, 1953.
 Randall, C. L., Baetz, R. W., Hall, D. W., and Birtch, P. K.: New York M. J. 50: 2525, 1950.

6

f

e

e

e

- 5. Potter, E. L.: Pathology of the Fetus and the Newborn, Chicago, 1953, The Year Book
- Publishers, Inc., chap. 7, p. 68.
 6. Kramer, E. E.: New York J. Med. 54: 2813, 1954.
 7. Lund, C. J.: New Orleans M. & S. J. 101: 443, 1949.
 8. Hughes, E. C., Van Ness, A. W., and Lloyd, C. W.: Am. J. Obst. & Gynec. 59: 1292,
- 9. Shapiro, S., and Unger, J.: Weight at Birth and Its Effect on Survival of the Newborn in the United States, Early 1950, U. S. Dept. of Health, Education and Welfare, Public Health Service, National Office of Vital Statistics 39: 24, 1954.

- nn the United States, Early 1950, U. S. Dept. of Health, Education and Welfare, Public Health Service, National Office of Vital Statistics 39: 24, 1954.

 10. Toback, M.: J. A. M. A. 146: 897, 1951.

 11. The American Academy of Pediatrics: A Round Table Discussion on Prematurity, J. Pediat. 8: 104, 1936. (Cited by Toback. 10)

 12. Hacker, E. M., Epperson, J. W. W., Priddle, H. D., and Longyear, H. W.: Am. J. Obst. & Gynec. 64: 644, 1952.

 13. Morrison, J. H.: Obst. & Gynec. 2: 297, 1953.

 14. Marchetti, A. A., and Menaker, J. S.: Am. J. Obst. & Gynec. 59: 1013, 1950.

 15. Bookstover, P. I.: Am. J. Obst. & Gynec. 61: 399, 1951.

 16. Taylor, E. S., Phalen, J. R., and Dyer, H. L.: J. A. M. A. 141: 904, 1949.

 17. Wallace, H. M., Roscoff, H., and Knoblock, H.: J. A. M. A. 146: 886, 1951.

 18. Eastman, N. J.: Am. Pract. 1: 343, 1947.

 19. Smith, G. G., Mackennon, C. F., and Molleson, A.: Bull. Mat. Welfare 2: 7, 1955.

 20. Darby, W. J., Bridgforth, E., Martin, M. P., and McGanity, W. J.: Obst. & Gynec. 5: 528, 1955.

 21. Tompkins, W. T.: in Lull, C. B., and Kimbrough, R. A., editors: Clinical Obstetrics, Philadelphia, 1953, J. B. Lippincott Company, pp. 163-251.

 22. Ferguson, J. H.: Am. J. Obst. & Gynec. 61: 603, 1951.

 23. Abramson, D., and Reid, D. E.: J. Clin. Endocrinol. 15: 206, 1955.

 24. Karlson, S.: Acta obst. et gynec. scandinav. 28: 209, 1949.

 25. Bundeson, H. N.: J. A. M. A. 157: 1384, 1955.

DURATION OF PREGNANCY FOR CLEFT PALATE CHILDREN*+

KENNETH R. LUTZ, A.M., ONAWA, IOWA, AND C. E. FRANCIS, M.D., LOMA LINDA, CALIF.

(From the Departments of Therapeutics and Obstetrics, College of Medical Evangelists, Loma Linda, California)

HIGHER incidence of premature births among cleft palate children was reported by Phair and others. 1, 2, 3 Suabedissen studied the duration of pregnancy for a large number of severely deformed children and noted little resemblance to the normal pregnancy duration curves. He concluded that the more severe the deformity the shorter the duration of pregnancy and suggested that though the deviation is small, if any, for the less severe deformities, they should be studied.

It was the purpose of this study to determine whether or not the length of the period of those pregnancies that result in children born with cleft palate is significantly shorter than the length of the period of those pregnancies that terminate with the birth of normal children.

Materials and Methods

The case records of all cleft palate cases admitted as patients to the Los Angeles County General Hospital and of the control group during the period beginning July 1, 1936, and ending Dec. 31, 1951, were studied.

A modification of the table prepared by Wylie and Amidon⁵ has been used to determine the duration of pregnancy in this study. The factors of birth weight and birth length were correlated with the time from the first day of the last menstrual period to the birth of the child.

Definition of Terms.—Unless otherwise stated, the term "duration of pregnancy" shall refer to the period of time from the first day of the last menstruation to the birth of the child.

The term "race" shall be used to specify the ethnic stock from which an individual has descended. Throughout this paper races have been considered as follows: White—any person of Caucasian ancestry; Negro—any person whose ancestry is of the black races of Africa; Mexican—any person who is the descendant of a Caucasian-American Indian blend, peculiar to Mexico.

Stillborn infants, infants with observable deformities other than eleft palate, delivered by cesarean section, delivered as a result of artificially induced labor, born to mothers less than 16 years of age, born to mothers with diagnosed diabetes, or born to mothers with venereal disease were excluded from this study of the duration of pregnancy.

The statistics of the several races, Caucasian, Mexican, and Negro, were considered separately.

The Control Group.—In order to determine the significance of these data it was necessary to compare them with data compiled from an average or nor-

^{*}A report of data presented to the University of Redlands, Redlands, Calif. senior author in partial fulfillment of the requirements for the Master of Arts Degree †Supported in part by the Bureau of Rehabilitation, State of California Department of

mal group of subjects. Sutton⁶ pointed out that the normal duration of pregnancy may not be constant and that it should be determined for each locality. Statistics of a control group of subjects were compiled from data collected in the same manner as for the study group. The data comprising the control group were compiled from the records of each child who was born in the Los Angeles County General Hospital immediately following the birth of those born with cleft palate, or immediately after 12:00 noon on the date of birth of those with cleft palate who were not born in the hospital.

The mean duration of pregnancy was determined for each group and compared with the mean duration of pregnancy of the respective control group and with the respective normal mean duration of pregnancy as reported by Hotelling and Hotelling.⁷ The significance of the "t" value was determined from the "Distribution of 't' Table" prepared by Fisher and Yates.⁸

The Findings

There were no significant differences in the mean duration of pregnancy of the various race groups included in the hospital control from that of the respective Hotelling and Hotelling statistics (Table I). The mean duration of pregnancy of the cleft palate groups was significantly shorter than that of the respective control groups. Though the duration of pregnancy of the Mexican Cleft Palate Group could not be considered significantly shorter than that of the respective hospital control group, it was measurably shorter (Table II). The mean duration of pregnancy of the Cleft Palate Negroes was 256 days. The sample was too small for statistical analysis, however.

TABLE I. ANALYSIS OF DURATION OF NORMAL PREGNANCY

	CAUC	ASIAN	MEX	MEXICAN		NEGRO	
	HOSPITAL CONTROL GROUP	HOTELLING AND HOTELLING CONTROL STATISTICS	HOSPITAL CONTROL GROUP	HOTELLING AND HOTELLING CONTROL STATISTICS	HOSPITAL CONTROL GROUP	HOTELLING AND HOTELLING CONTROL STATISTICS	
Number	37	537	53	56	44	28	
Mean of distribution	279.2	281.4	274.8	277.3	276.6	276.3	
Standard deviation	6.0	10.8	8.2	14.4	6.4	9.2	
t between variables Significance (P) be-		1.929		1.122		0.147	
tween variables		0.1		0.3		0.9	

TABLE II. ANALYSIS OF DURATION OF CLEFT PLATE PREGNANCY

	(CAUCASIAN			MEXICAN		
	CLEFT PALATE GROUP	HOSPITAL CONTROL GROUP	HOTELLING AND HOTELLING CONTROL STATISTICS	CLEFT PALATE GROUP	HOSPITAL CONTROL GROUP	HOTELLING AND HOTELLING CONTROL STATISTICS	
Number	70	37	537	28	53	56	
Mean of distribution	268.2	279.2	281.4	269.2	274.8	277.3	
Standard deviation	18.2	6.0	10.4	13.8	8.2	14.4	
t between variables Significance (P) be-		5.893	5.893		1.944	2.485	
tween variables		0.001	0.001		0.1	0.02	

The mean duration of pregnancy of the Mexican and Negro control groups was significantly shorter than that of the Caucasian control group. There were

no significant differences in the mean duration of pregnancy of the various cleft palate race groups (Tables III and IV).

TABLE III. ANALYSIS OF THE DURATION OF PREGNANCY OF THE VARIOUS RACE GROUPS OF THE HOSPITAL CONTROL GROUP

	HOSPITAL CONTROL GROUP			
	CAUCASIAN	MEXICAN	NEGRO	
Number	37	53	44	
Mean of distribution	279.2	274.8	276.6	
Standard deviation	6.0	8.2	6.4	
between variable Caucasian and		3,709	2.600	
between variable Mexican and			1.192	
Significance (P) between variable Caucasian and	40-40-40-40	0,001	0.02	
Significance (P) between variable Mexican and			0.3	

TABLE IV. ANALYSIS OF THE DURATION OF PREGNANCY FOR THE CAUCASIAN AND MEXICAN CLEFT PALATE GROUPS

	CLEFT PALATE GROUP		
	CAUCASIAN	MEXICAN	
Number	70	28	
Mean of distribution	268.2	269.2	
Standard deviation	18.2	13.8	
t between variables		0.291	
Significance (P) between variables	size size har sar	0.8	

Discussion of the Findings.—The mean duration of pregnancy of the several racial Hospital Control Groups varied slightly from that reported by Hotelling and Hotelling but the differences were not significant.

The mean duration of pregnancy of the various groups of cleft palate cases was shorter than the mean duration of pregnancy of the respective control groups. This was considered significant for the Caucasian Cleft Palate Group and slightly significant for the Mexican Cleft Palate Group.

The short duration of pregnancy of persons with cleft palate may be interpreted to indicate that there is a relationship between the factor that caused the cleft palate and that factor which caused the premature birth. The relationship of the cause of cleft palate and the cause of premature or early birth is not indicated by this statistical study. It is suggested that the relationship between prematurity and cleft palate should be investigated by controlled animal experimentation in the laboratory.

Summary and Conclusions

The data for this study were compiled from the case records of the Los Angeles County General Hospital. The duration of pregnancy was determined for 102 patients with cleft palate whose hospital records contained the data necessary. The mean duration of pregnancy was determined for each of the several race groups and compared with the mean duration of pregnancy of a respective group of normal persons selected as a control from persons born in the hospital during the period studied. The significance of the mean differences was determined by the "t" test.

It was shown that:

- 1. The mean duration of the pregnancies that terminate with the birth of a child with cleft palate is significantly shorter than the mean duration of the pregnancies that terminate with the birth of a normal child.
- 2. There is no significant difference in the mean duration of pregnancy for children born with cleft palate of the several races.

References

- 1. Phair, Gretchen Mueller: J. Speech & Hearing Disorders 12: 412, 1947.

- Phair, Gretchen Mueller: J. Speech & Hearing Disorders 12: 412, 1947.
 De Voss, Henry: Speech Monographs 19: 308, 1952.
 Worchester, J., Stevenson, S. S., and Rice, R. C.: Pediatrics 6: 208, 1950.
 Suabedissen, Hans: Zentralbl. Gynäk. 62: 751, 1938.
 Wylie, Burdett, and Amidon, Blaine F.: Am. J. Obst. & Gynec. 61: 193-196, 1951.
 Sutton, David Harvey: M. J. Australia 1: 611, 1945.
 Hotelling, Harold, and Hotelling, Floy: Am. J. Obst. & Gynec. 23: 643, 1932.
 Fisher, Ronald A., and Yates, Frank: Statistical Tables for Biological, Agricultural, and Medical Research, London, 1943, Oliver and Boyd, Ltd., p. 30.

COMMENTS ON THE RICHARDSON PREGNANCY TEST AND THE RAPP-RICHARDSON SALIVA PRENATAL SEX DETERMINATION TEST

W. G. Dobson, M.D., and A. G. Gornall, Ph.D., Toronto, Ontario (From the Department of Pathological Chemistry, University of Toronto)

THE Richardson test for the diagnosis of pregnancy^{1, 2} is stated to depend on the demonstration, either with 2,4-dinitrophenylhydrazine or with meta-dinitrobenzene, of increased amounts of free estrone in urine during the early weeks of gestation. In the hands of other workers³⁻¹⁴ the test has proved less reliable than its originator claimed even though a number of improvements in the technique have been suggested. Stimmel⁹ points out that early pregnancy urine does not contain enough free estrone to give a positive Zimmermann reaction. Most workers, however, have used the dinitrophenylhydrazine reagent and Rapp¹⁵ has recently defended the method with some vigor. It seems desirable therefore that our observations on this test should be reported.

Results in the Diagnosis of Pregnancy

The test was carried out as described by Richardson, with the use of 95 per cent alcohol to dissolve the 2,4-dinitrophenylhydrazine (DNPH). The urine specimens were obtained mainly from clinic patients, some were first morning specimens but many were afternoon urines. All were tested while fresh and no difference in the reliability of the test was evident between specimens collected at these different times. Results are recorded in Table I.

TABLE I

TYPE OF PATIENT	NUMBER POSITIVE	NUMBER NEGATIVE	OVER-ALL ACCURACY
Nonpregnant	43	37	46.5%
Pregnant:			
0- 8 weeks	5	1 1	=0.0/
8-12 weeks	8	4	72%
12-32 weeks	17	6	76%
32-40 weeks	43	15	74%

During this work it was thought that a urine "blank" from which free estrone had been removed would make a suitable background for reading the test in a spectrophotometer. A portion of fresh urine was therefore extracted with ether and then compared in the Richardson test with the unextracted specimen. The "blank" gave the same result as the specimen. When chloroform was used instead of ether the "blank" often gave a stronger positive than the specimen. If two or three chloroform washes were used, the intensity of the reaction in the extracted urine was always enhanced.

One of us¹⁶ had made a study of the reaction between steroid hormones and DNPH. Among the substances tested estrone was one of the least reactive.

1

There was reason to doubt that Richardson's procedure detects estrone at all. Not only was it uncertain that the method separates free estrone from other reactive substances but the quantity of free estrone present seemed far too small to be demonstrated with the reagent employed.

Evidence of the Doubtful Value of the Extraction Procedure

The phenolic nature of the estrogens has long been used to effect their partition into alkaline solutions from ether-soluble steroids lacking an acidic radical. The separation of estrone, which is least hydrophilic of the three estrogens, requires special care.^{17, 18, 19} Although estrone is less soluble in chloroform than in ether, the concentration of alkali required to keep it quantitatively in the aqueous phase is about 1 N. As Stimmel⁹ points out, the addition of two drops of N/2 sodium hydroxide does not assure the requisite alkalinity for this separation. It is highly probable that the small amount of "free" estrone in urine is in most instances lost in the chloroform extract. Larger amounts of conjugated derivatives of estrone and of many other steroids would of course be left behind in the aqueous phase.

Schaible and Schlüren⁶ found that omitting the chloroform extraction made no difference to the outcome of the test in most cases. We have found that an ether wash makes no difference to the test and a chloroform wash tends to produce or enhance a positive reaction.

Evidence That the Estrone Present in Small Volumes of Pregnancy Urine Is Not Detectable by DNPH

According to Richardson the DNPH test depends on the presence of "a substantial amount of free estrone in the urine of pregnant women." Evidence from the literature is summarized in Table II and fails to support such a view.

TABLE II

AUTHORS	TYPE OF URINE	FRACTION ANALYZED	MG. PER DAY
Cohen, Marrian, and Watson ²⁰	Second trimester	Total estrone Free estrone	Approx. 1 <1% of total
Smith and Smith ²¹	Third trimester	Total estrone (+ estradiol?)	0.5 - 0.96'
Bachman and Pettit ²²	Third trimester	Total estrone (+ estradiol?)	0.3-2.8
Hain ²³	Third trimester	Total free estrogens	< 0.1
Stimmel ²⁴	First trimester	Total estrone	0.05 - 0.25
Oneson and Cohen ²⁵	Third trimester	Total estrone Free estrone	0.5-1.5/L. <15 mcg./L.

It appears that the urine of pregnant women, even in the third trimester, contains much less than 0.1 mcg. of free estrone per ml. of urine. Gornall and Macdonald¹6 found that in 87 per cent methanol the reaction of estrone with DNPH at room temperature showed a molar extinction coefficient of about 200. It could be calculated that at least 100 mcg. of estrone would be necessary to give a visible color. To test this point, increasing amounts of estrone were added to 2 ml. of water (or negative urine) and it was found that the Richardson test became positive when about 120 mcg. was present. It is estimated

that the free estrone (indeed even the total estrone) in 2 ml. of early pregnancy urine is probably less than ½,000 the amount necessary to produce a visible color with DNPH. No proof that estrone is the substance being demonstrated in the Richardson test has ever been published, though Merkel¹ refers to a "personal communication" from Rapp that this detail had been checked.

Peculiar Effect of pH in the Richardson Test

Fischer¹⁰ reported that exercise caused a positive Richardson test in non-pregnant women. Plattner and Hadavi¹³ felt it advisable to adjust the pH of all urines to 7.0 before carrying out the test. Rapp¹⁵ reported that some lots of chloroform (it would be interesting to know their acid content) caused false positive reactions. He stated that the optimum alkalinity for separation of estrone is pH 11, the optimum pH for coupling with DNPH is between 3 and 4, and claimed that the addition of the reagents as prescribed assures these conditions. This presumes a remarkable constancy of urine pH and buffer capacity.

We have measured the pH of the urine samples after neutralization of the alkali with sulfuric acid and related this pH to the outcome of the test. Those urines which gave a positive test were found to have, just prior to the addition of the DNPH reagent, pH values ranging from 1.6 to 4.3; results for the negative urines ranged from 3.3 to 5.8. These values bore very little relation to the pH of the original urine. With rare exceptions the test was found to be negative if the pH at this stage was above 4.0 and positive if below 4.0. An adjustment of the pH across this dividing line would render a negative test positive or a positive test negative. Results on the urine from 45 pregnant and 50 nonpregnant women are shown in Table III.

TABLE III

PREGNANT		NONPREGNANT	
Positive Richardson test	28	Positive Richardson test	29
pH under 4.0	27	pH under 4.0	28
pH 4.0 or over	1	pH 4.0 or over	1
Negative Richardson test	17	Negative Richardson test	21
pH under 4.0	1	pH under 4.0	4
pH 4.0 or over	16	pH 4.0 or over	17

Comment

It seems impossible that the success of the Richardson test in some hands could depend on the presence of estrone. If under the rigid conditions defined by Rapp the test has some basis in fact, it would be interesting to know in what respect the urine in early pregnancy differs from that of nonpregnant women. We are not aware of any evidence that the first morning urine of pregnant women is consistently more acid or less highly buffered.

It is possible that pregnancy urine contains larger amounts of some other substances reacting with DNPH. Relatively large amounts of conjugated corticosteroids are present in urine and would remain in the aqueous phase during a chloroform wash. At room temperature Δ^4 -3 ketosteroids form hydrazones rapidly with DNPH, but most steroid conjugates require the prior reduction of this group to a C-3 hydroxyl. Conjugated steroids with a C-20 keto group could react to some extent at room temperature and might con-

tribute to a positive test, but we have no proof that this happens under the conditions prescribed. It is known of course that increased excretion of adrenal steroids occurs in pregnancy; the rise, however, is not invariable and on the average is barely significant in the first trimester. We have observed that the urine of a nonpregnant patient receiving 50 mg. of cortisone daily consistently gave a strong positive test. A strong test was obtained also on all urines from a patient receiving a ketogenic diet. It appears that most, if not all, urines contain substances which will react with DNPH if the pH conditions are right. Pregnancy urine may tend to contain more of these substances.

The Rapp-Richardson Saliva Prenatal Sex Determination Test

The Richardson test when applied to the saliva of a woman in the sixth or seventh month of pregnancy is stated to give a positive test when a male or a negative test when a female fetus is being carried.²⁶ Rapp and Richardson have suggested that some androgenic substance, coming presumably from the fetus, is being identified. It is curious that a method which was designed to eliminate nonestrogenic substances is here regarded as capable of detecting them.

Our observations were made on a series of 76 patients attending the prenatal clinic of the Toronto General Hospital. Each patient, in the third trimester, received an instruction sheet, a square of paraffin, and a clean bottle. Approximately 15 ml. of saliva was obtained in each case. Samples were refrigerated immediately after collection and tested within 24 hours. The results of this study are recorded in Table IV.

TABLE IV

RESULTS	NUMBER OF PATIENTS	MALE CHILD	FEMALE CHILD	ACCURACY
Positive tests:				
Strong	21	11	10	52%
Medium	21	8	13	38%
Weak or uncertain	10	5	5	50%
Negative tests	24	11	13	46%
Over-all accuracy				46.5%

It can be noted that the reliability of the test at any level of intensity has been in our hands about that to be expected from tossing a coin.

To check the suggestion that androgens may be responsible for the positive tests, 100 ml. pooled collections of positive- and negative-reacting saliva were extracted and analyzed for 17 ketosteroids. Neither extract contained demonstrable amounts of material giving a Zimmermann reaction. A similar test of adult male saliva was also negative. The outcome of the saliva test was found to be sensitive to pH differences as in the case of the urine test.

Summary

The Richardson pregnancy test is questioned both as to its reliability and the theoretical basis on which it was proposed.

In our hands an accuracy of about 75 per cent in pregnant patients and 47 per cent in nonpregnant women was obtained.

Evidence is presented that the method of extraction does not effect any separation or purification of an estrone fraction and even if it did the amount of free estrone in pregnancy urine is much too small to be detected with 2,4dinitrophenylhydrazine.

The Rapp-Richardson saliva prenatal sex determination test is subject to similar criticism and had in our hands an accuracy which indicated that the result was in no way determined by the sex of the fetus.

References

- Merkel, R. L.: AM. J. OBST. & GYNEC. 60: 827, 1950.
 Richardson, G. C.: AM. J. OBST. & GYNEC. 61: 1317, 1951.
 Halpern, E. P., Gross, M. L., and Brody, H.: Proc. Soc. Exper. Biol. & Med. 80: 182, 1952.
- 4. Cuboni, E., and Ranfagni, R.: Boll. soc. ital. biol. sper. 28: 998, 1952.

- 1952.
 4. Cuboni, E., and Ranfagni, R.: Boll. soc. ital. biol. sper. 28: 998, 1952.
 5. Neumeister, E.: Xrztl. Wchnschr. 7: 1054, 1952.
 6. Schaible, G., and Schlüren, E.: Deutsche med. Wchnschr. 77: 1609, 1952.
 7. Horwitt, B. N., and Segaloff, A.: J. A. M. A. 151: 406, 1953.
 8. Levens, H. E.: Klin. Wchnschr. 31: 136, 1953.
 9. Stimmel, B. F.: Am. J. Obst. & Gynec. 65: 633, 1953.
 10. Fischer, R. H.: M. Ann. District of Columbia 22: 62, 1953.
 11. Fischer, R. H., and McColgan, S. P.: Am. J. Obst. & Gynec. 65: 628, 1953.
 12. Rolandi, L., and De Dominicis, E.: Ann. ostet. e ginec. 76: 901, 1954.
 13. Plattner, F., and Hadavi, S.: München. med. Wchnschr. 96: 1020, 1954.
 14. Roth, L. G., and Leonard, W. G., Jr.: U. S. Armed Forces M. J. 5: 83, 1954.
 15. Rapp, G. W.: Am. J. Obst. & Gynec. 67: 411, 1954.
 16. Gornall, A. G., and Macdonald, M. P.: J. Biol. Chem. 201: 279, 1953.
 17. Friedgood, H. B., and Garst, J. B.: In Pincus, G., editor: Recent Progress in Hormone Research, New York, 1948, Academic Press, Inc., vol. II, p. 31.
 18. Engel, L. L.: In Pincus, G., editor: Recent Progress in Hormone Research, New York, 1950, Academic Press, Inc., vol. V, p. 335.
 19. Brown, J. B.: Biochem. J. 60: 185, 1955.
 20. Cohen, S. L., Marrian, G. F., and Watson, M.: Lancet 1: 674, 1935.
 21. Smith, G. V., and Smith, O. W.: Am. J. Obst. & Gynec. 39: 405, 1940.
 22. Bachman, C., and Pettit, D. S.: J. Biol. Chem. 138: 689, 1941.
 23. Hain, A. M.: J. Endocrinol. 3: 10, 1942.
 24. Stimmel, B. F.: J. Biol. Chem. 165: 73, 1946.
 25. Oneson, I. B., and Cohen, S. L.: Endocrinology 51: 173, 1952.
 26. Rapp, G. W., and Richardson, G. C.: Science 115: 265, 1952.

EXPERIMENTAL AMNIOTIC FLUID INFUSION

A Preliminary Report

ROBERT M. HUNTER, M.D., JOHN C. SCOTT, PH.D., JOHN P. SCHNEIDER, V.M.D., AND JOHN A. KRIEGER, M.D., PHILADELPHIA, PA.

(From the Division of Women and Physiology, Hahnemann Medical College and Hospital)

NUMEROUS maternal deaths, said to have been the result of amniotic fluid embolism, have been reported in the literature over the past fourteen years. The senior author has felt many of these deaths could be explained by more common clinical entities, such as hemorrhage, heart failure, cerebral accidents, or aspiration of gastric content. Others^{1, 2} have expressed themselves in a similar manner.

Tunis³ analyzed 25 maternal deaths said to have been caused by amniotic fluid embolism. This group included the original 8 cases reported by Steiner and Lushbaugh⁴ in 1941, which led them to postulate amniotic fluid embolism as a cause for sudden maternal death. Tunis rejected twenty of these twenty-five cases on the ground that there could be demonstrated an adequate cause for sudden death, other than amniotic fluid embolism. The remaining five cases he refused to classify stating that the autopsy findings were inadequate.

Tunis' opinion as to the validity of the interpretation of the pulmonary findings at postmortem in the cases analyzed is worth quoting in full: "We refuse to recognize the microscopic findings as reported in all cases because of the following factors: During pregnancy the capillaries all over the body and not alone in the lungs undergo changes from slight lability toward paresis. This causes a disturbance in the exchange of fluids and other matter between elements in and out of the capillaries. The blood remains ten times as long in the capillaries of the pregnant woman as in the capillaries of the nonpregnant. The endothelium of the capillary wall will show a greater permeability during pregnancy which is caused by a loosening of the endothelial cells. As a result, exudation or even bleeding per diapedesis is more likely to occur. This will explain in large part the postmortem findings in the lungs. As stated before, and I would repeat it again, various decidual and placental cells may appear in the lung capillaries without doing any damage to the body." Wilson² discussing Watkins' paper, expressed similar views.

Years before Steiner and Lushbaugh's paper, Warden⁵ in 1927 had subjected 10 female rabbits to intravenous injections of amniotic fluid, blood, and debris obtained from a doe rabbit at term at cesarean section and failed to kill 7. Only one of the 3 rabbits that died had been injected with "relatively clear amniotic fluid." Postmortem examination of this rabbit "failed to demonstrate a satisfactory cause of death." The other 2 rabbits that died did so of gross pulmonary embolic processes, the result of blood clots and organized debris.

Following Steiner and Lushbaugh's report of 1941, much animal experimentation referable to amniotic fluid embolism has been carried out. In 1949

they with Frank⁶ killed dogs by the intravenous injection of unfiltered amniotic fluid mixed with meconium obtained from newborn dead babies. They believed the cause of death to be pulmonary embolism and considered the meconium present in the amniotic fluid to be the agent that induced the embolic process.

We are not impressed by the possibility of a similar concentration of meconium and amniotic fluid entering the circulation of a pregnant woman via the uterine sinus, and hold the same view for Schneider's^{7, 8} interesting and extensive experiments with meconium amniotic fluid infusion in dogs.

In 1951, Page, Fulton, and Glendening,⁹ attempting to explain the hemorrhagic states occurring in certain cases of extensive premature separation of the placenta, in which some defect in the clotting mechanism was evident, produced in vivo defibrinization in dogs by the intravenous injection of homogenized aqueous extract of human placenta. They postulated that the defect in the clotting mechanism was due to the presence of thromboplastin in the placental extract. From this we might theorize that amniotic fluid is the vehicle in which the thromboplastin carried by the bits of placenta or decidual tissue enters the general circulation with resulting defibrination and hemorrhage.

The relative frequency with which premature separation of the placenta is associated with hemorrhage and defibrination makes the theory of Page and his associates logical. Maternal death under such circumstances is, however, a far cry from the sudden and bizarre deaths reported in the literature and earmarked as due to amniotic fluid embolism.

In a paper published in 1953, Reid, Weiner, and Roby¹⁰ theorized that intractable postpartum hemorrhage unexplained on a physical basis and revealing afibrinogenemia might be secondary to what they chose to call "amniotic fluid infusion." With this paper in mind, it seemed appropriate that the following two simple experiments be undertaken. To the best of our knowledge, similar experiments have not been performed.

Erneriment 1

A pregnant bitch, at term, weighing 6.4 kilograms, was anesthetized with intravenous pentobarbital sodium and blood drawn for coagulation and prothrombin time determinations. When the abdomen was opened, under aseptic technique, it was found that one horn of the bicornuate uterus contained one pup and the other horn, two pups. The anterior uterine musculature over each pup was incised for a distance of 1 or 2 cm. and the resulting bulging membranes tapped with a 19 gauge needle, and as much amniotic fluid withdrawn as possible. A total of 65 c.c. of clear amniotic fluid was obtained in this manner. The uterine musculature and the abdomen were then closed. The 65 c.c. of aspirated amniotic fluid was injected into a vein of the forepaw of the bitch over a 15 minute period. The pups were alive at the completion of the anesthesia.

Blood was drawn 15, 30, and 90 minutes after completion of the amniotic fluid infusion for coagulation and prothrombin time determinations. The bitch survived to die undelivered, 48 hours later while in labor. During the post-operative observation there was no abnormal bleeding from the vagina or abdominal wound and postmortem revealed the cause of death to have been ruptured uterus. Free blood in the peritoneal cavity was clotted.

The normal coagulation time in the dog is 1.5 to 2.5 minutes; the normal prothrombin time in the dog is 6 seconds. This compares to a coagulation time of from 3 to 8 minutes and a prothrombin time of from 12 to 14 seconds in the human (Table I).

TABLE I. COMPARISON OF COAGULATION AND PROTHROMBIN TIMES IN DOG AND MAN

Coagulation time in the dog	1.5-2.5 minutes
Prothrombin time in the dog	6 seconds
Coagulation time in the human	3-8 minutes
Prothrombin time in the human	12-14 seconds

Table II shows the coagulation time and the prothrombin time in bitch No. 1 before and after the amniotic fluid infusion. It will be noted that the coagulation time remained within or below normal limits. The blood drawn for prothrombin time was taken in an oxalated tube containing the usual 0.5 c.c. sodium oxalate solution. To this was added the usual $4\frac{1}{2}$ c.c. of blood. As noted, clotting in all specimens made prothrombin estimations impossible.

Table II. Coagulation and Prothrombin Times in Experiment 1 Before and at Various Times After Infusion With Amniotic Fluid

Preinfusion coagulation time	1.45 minutes
Preinfusion prothrombin time	blood clotted
15 minutes postinfusion coagulation time	1.15 minutes
15 minutes postinfusion prothrombin time	blood clotted
30 minutes postinfusion coagulation time	1.05 minutes
30 minutes postinfusion prothrombin time	 blood clotted
90 minutes postinfusion coagulation time	1 minute
90 minutes postinfusion prothrombin time	blood clotted

Experiment 2.—

A pregnant bitch, weighing 17½ kilograms, on the fifty-fourth day of gestation, was anesthetized with 7 e.c. of Pentonesin (a mixture of pentobarbital sodium and Nephensin, a curarelike preparation) intravenously. After 15 minutes the femoral arteries and veins in both legs were exposed. A Lilly Capacitance Manometer was connected to the right femoral artery. The left femoral vein was isolated and blood drawn for coagulation and prothrombin time. One hour after induction of anesthesia a cesarean section under aseptic precautions was performed and 6 pups were found.

The amniotic fluid of each of the 6 amniotic sacs was collected and strained through four thicknesses of ordinary surgical gauze. Four pups showed no signs of life and the amniotic fluid in each case was heavily stained with meconium. The remaining 2 pups made feeble attempts at respiration but did not survive. The amniotic fluid contained in the amniotic sacs of the latter 2 pups was relatively clear.

A total of 172 c.c. of amniotic fluid was obtained. The entire amount was injected into the exposed left femoral vein over a period of four and one-half minutes. Blood was drawn for coagulation and prothrombin time determinations 15, 30, and 90 minutes after completion of the amniotic fluid infusion. No abnormal bleeding from the vagina, abdominal wound, or wounds in the thighs occurred. Blood pressure readings remained within normal limits at all times. The bitch did well postoperatively and still survives.

Table III shows the coagulation time and the prothrombin time in bitch No. 2 before and after the amniotic fluid infusion.

As in Experiment 1, the coagulation time remained at or below the normal limits. Also, as in Experiment 1, blood drawn for prothrombin time determination elotted in all tubes. We do not have actual figures on prothrombin estimation. We were cognizant of the normal decrease in coagulation and prothrombin time in the dog over the human, but failed to take into consideration the probable increase in epinephrine output under stress, with a resulting increase in prothrombin output. In subsequent experiments, increasing amounts of sodium

oxalate in proportion to the amount of blood were used. We believe, however, that it is fair to conclude that the rapid clotting in the presence of standard amounts of sodium oxalate is inconsistent with afibrinogenemia.

TABLE III, COAGULATION AND PROTHROMBIN TIME IN EXPERIMENT 2 BEFORE AND VARIOUS TIMES AFTER INFUSION WITH AMNIOTIC FLUID

Preinfusion coagulation time	1.05 minutes
Preinfusion prothrombin time	blood clotted
15 minutes postinfusion coagulation time	1 minute
15 minutes postinfusion prothrombin time	blood clotted
30 minutes postinfusion coagulation time	1 minute
30 minutes postinfusion prothrombin time	blood clotted
90 minutes postinfusion coagulation time	stat.
90 minutes postinfusion prothrombin time	blood clotted

Summary

Two bitches, at or near term, were subjected to an infusion of practically the entire amount of their amniotic fluid. In one bitch, the amniotic fluid was clear and uncontaminated with meconium or blood. In the other, the amniotic fluid was heavily stained with meconium, the result, we believe, of intrauterine death of her pups secondary to anesthesia.

In one bitch, the quantity of amniotic fluid infused amounted to more than 10 per cent of the total estimated blood volume and was injected slowly (65 c.c. in 15 minutes). In the other, the amount of amniotic fluid infused amounted to more than 12 per cent of the total blood volume and was injected rapidly (172 c.c. in $4\frac{1}{2}$ minutes).

Both bitches survived the amniotic fluid infusion. Neither revealed any tendency toward abnormal bleeding. The blood coagulation time remained at normal or below normal limits. Prothrombin time apparently remained within normal limits. The blood pressure remained unchanged.

Conclusion

From the experiments described, it appears that:

- 1. In the pregnant bitch, at least, amniotic fluid infusion, per se, is not a cause of sudden death.
- 2. Autoinfusion of the entire amount of amniotic fluid of the bitch, at or near term, does not act as a trigger mechanism in the production of the pathological entity known as afibrinogenemia.

- 1. Mendelson, C. L.: Am. J. Obst. & Gynec. 55: 911, 1948.
 2. Wilson, J. R.: Discussion of Watkins, E. L.: Am. J. Obst. & Gynec. 56: 995, 1948.
 3. Tunis, B.: Am. J. Obst. & Gynec. 64: 72, 1952.
 4. Steiner, P. E., and Lushbaugh, C. C.: J. A. M. A. 117: 1245, 1941.
 5. Warden, M. R.: Am. J. Obst. & Gynec. 14: 292, 1927.
 6. Steiner, P. E., Lushbaugh, C. C., and Frank, H. A.: Am. J. Obst. & Gynec. 58: 802, 1949.
 7. Schneider, C. L.: Am. J. Obst. & Gynec. 65: 245, 1953.
 8. Schneider, C. L.: Am. J. Obst. & Gynec. 69: 758, 1955.
 9. Page, E. W., Fulton, L. D., and Glendening, M. B.: Am. J. Obst. & Gynec. 61: 1116, 1951.
- Reid, D. E., Weiner, A. F., and Roby, C. C.: Am. J. Obst. & Gynec. 66: 465, 1953.

STUDIES ON PERITONEAL FLUID IN THE PREGNANT RAT*

JACQUES PADAWER, Ph.D.,** AND ALBERT S. GORDON, Ph.D., NEW YORK, N. Y. (From the Department of Biology, Graduate School of Arts and Science, New York University)

ALTERATIONS have been reported to occur in the number of certain of the peripheral blood cells during pregnancy. Thus the presence of anemia in pregnant animals¹ and women² has been well demonstrated. In turn, various anemic states are associated with significant changes in the phagocytic activity of the blood leukocytes.³⁻⁷

Since peritoneal fluid has been shown to be well suited for quantitative studies of a variety of cellular elements such as eosinophilic leukocytes, reticulo-endothelial elements, and mast cells, 8-11 a study has been made of the changes undergone by this fluid during pregnancy in the rat. Parameters examined have included the volume of, and cellular numbers within, the peritoneal fluid of pregnant rats on standard or on iron-enriched diets; the phagocytic activity of the free macrophages of the peritoneal fluid has also been assessed.

Materials and Methods

1. Animals Used.—Virgin adult female rats (150-200 grams) of a modified Long-Evans strain were used. Vaginal smears were taken to determine when the animal was in proestrus, at which time it was placed in a cage with a male for a period of 12 to 24 hours to allow for mating. The presence of sperm in the vaginal smear was found to be an unreliable index of successful mating and the mechanical stimulation inherent in the smearing procedure resulted sometimes in pseudopregnancy. It was noted, however, that, when known fertile males were used, almost 100 per cent successful matings ensued. Daily weighings were done during pregnancy and all animals were checked at autopsy for embryos in the uterine horns.

Fifteen pregnant animals on a standard diet were studied: 5 at ten days, 1 at fifteen days, and 9 at twenty days of the gestation period. Nine additional animals on a high-iron intake were examined on the twentieth day of pregnancy.

2. Diets.—All animals were reared on a powdered mix containing nine parts of calf meal† and one part meat scraps‡ enriched with cod-liver oil. Green leafy vegetables were supplied approximately once a week. This constituted the standard ration. For the iron-supplemented group, ferric chloride was dissolved in the drinking water, enough being added to impart a rich brownish-red color to the water. Whenever the iron came out of solution as an amorphous reddish precipitate (probably ferric hydroxide), a new FeCl₃

^{*}Supported, in part, by a grant in aid from the American Cancer Society upon recommendation of the Committee on Growth of the National Research Council.

^{**}Postdoctoral Research Fellow of the American Heart Association. Present address: Department of Biochemistry, Albert Einstein College of Medicine, Yeshiva University, New York, N. Y.

 $^{^{\}dagger}\text{Calf}$ meal was obtained from the Cooperative Granges League Federation Exchange, Inc., Ithaca, N. Y.

tObtained from Goetz and Co., New York, N. Y.

solution was substituted. This iron supplement was given for from 5 to 8 days prior to the time of sampling, i.e., the twentieth or twenty-first day of gestation. These animals gained weight normally and no toxic effects of the ferric chloride were noted.

3. Technical Procedures.—All the animals were killed by exsanguination under light ether anesthesia. The abdominal cavity was opened by a midline incision with care to avoid loss of fluid. A sample of peritoneal fluid was diluted 1:20 with Randolph fluid¹² in a white blood cell pipette. Another small sample was deposited on a slide and smeared as for blood preparations. The balance of the fluid obtainable from the cavity was carefully withdrawn with a medicine dropper, transferred to a small vial, and the amount carefully measured.³ From the cellular concentrations and fluid volumes measured, absolute cell numbers were calculated for individual animals.

The density of peritoneal fluid was determined as follows. Fluid was obtained as described above and centrifuged at high speeds to sediment the cells. A pipette to contain 20 c.mm. was then weighed before and after being filled with cell-free peritoneal fluid. The density was then calculated as weight of fluid per unit volume. Density measurements were also carried out on the gravid uterus. Both uterine horns were removed together with the developing embryos and weighed. The entire organ was then submerged into a measured volume of water contained in a 100 ml. graduate cylinder with care to free any air bubbles that might have become trapped in the process. The volume of the structure was then taken as that of the displaced water. Density measurements of the peritoneal fluid and of the gravid uterus were carried out for 2 rats near term.

Statistical analyses of the data were performed according to standard procedures.¹³

Results

The data have been summarized in Table I. The amount of fluid obtainable from the peritoneal cavity increases with pregnancy, reaching values approximately 4 times that for virgin animals of the same age. By inspection, it is clear that during pregnancy much more fluid is present than would be required for lubrication of internal organs. The amount of fluid obtainable from 6 nongravid females of body weight approximately equal to that of the 20 day pregnant animals (including weight of the embryos) averaged 0.21 ml. as compared to 0.37 ml. and 0.90 ml. on the tenth and twentieth day of the gestation period, respectively. In all cases, the peritoneal fluid was clear and did not clot at room temperature. Concentrations of mononuclear cells, eosinophils, and mast cells were lower than in nongravid females, but calculations of absolute numbers showed this to represent a dilution effect; all cellular types were actually increased in numbers during the course of gestation.

Eosinorrhexis was demonstrable in all groups. The uptake of degenerating eosinophils by free macrophages of peritoneal fluid was considerably greater during the last stages of pregnancy than in the earlier phases or in nongravid animals as shown by the ratios of macrophages containing ingested eosinophil material (Me) to unphagocytized degenerating eosinophils (e).

Dietary iron supplements did not appear to affect either fluid volume or cellular concentrations to any striking extent. There was a dramatic reversal of phagocytic activity, however, as expressed by the Me/e data.

Density measurements on peritoneal fluid and gravid uterus yielded average values of 1.005 Gm. per cubic centimeter and 1.06 Gm. per cubic centimeter, respectively.

TABLE I. PERITONEAL FLUID VALUES DURING PREGNANCY IN THE RAT (MEANS ± STANDARD ERRORS)

	I. VIRGIN FEMALI	ES†	20) 1	GNANT DAYS RD DIE	,	2	0	EGNANT DAYS DIET)	,
Body weight (grams)		(5)‡	248.0 :	+	8.0	(4)	247.0	+	7.7	(9)
Fluid volume (c.c.)	0.21 ± 0.085	(6)	0.90	<u>+</u>	0.14	(9)	0.79	+	0.086	(9)
Numbers per c.mm.										
WBC × 10-3	96.3 ± 5.97	(34)	64.6	±	8.44	(9)	58.9	\pm	7.28	(9)
E × 10-3	27.5 ± 2.41	(34)	18.4	+	3.31	(9)	21.5	+	2.65	(9)
M × 10-3	2.90 ± 0.23	(34)	1.10 :	+	0.28	(9)	1.18	+	0.07	(9)
е	225.0 ± 50.0	(16)	48.9	+	16.7	(9)	106.0	+	33.5	(9)
Me	175.0 ± 28.6	(16)	223.0	+	35.2	(9)	97.8	+	25.9	(9)
e + Me	400.0 ± 60.7	(16)	261.0	+	42.5	(9)	204.0	\pm	48.2	(9)
Absolute numbers										
WBC × 10-3	20,200§		53,400 :	+	9.500	(9)	42,300	+	4,890	(9)
E × 10-3	5,780		13,300 :			(9)	16,000	+	2,160	(9)
M × 10-3	609		1,490 :		684	(9)	899	+	78.5	(9)
e × 10-2	473		1,955 :		421	(9)	736	+	271	(9)
Me × 10-2	368		1,950		921	(9)	727	+	141	(9)
e + Me × 10-2	841		2,270		457	(9)	1,490	+	399	(9)
Me/e	1.93 ± 0.64	(16)	9.80 :	+	3.60	(9)	1.61	+	0.45	(9)
% E		(34)	28.5	+	3.70	(9)	38.1	+	4.52	(9)

*The following abbreviations are used: WBC = eosinophils + mononuclear cells (lymphocytic and macrophagic elements), excluding mast cells; E = eosinophilic leukocytes; M = mast cells; e = nonphagocytized degenerating eosinophils; Me = macrophages containing phagocytized eosinophilic material; e + Me = total eosinophil breakdown.

†Values for nonpregnant animals represent pooled data from other experiments.

‡Numbers of animals used are indicated in parentheses.

 $\S Absolute$ cellular numbers for this group were calculated as mean cellular concentration \times mean fluid volume rather than for individual animals.

Comment

The function of peritoneal fluid has been commonly thought to be confined to lubrication. This may well be its only role in nonpregnant rats, but the amounts of fluid collecting in the abdominal cavity during pregnancy far exceed the quantity necessary to reduce friction between contiguous structures; the fluid virtually floods the cavity. This increase in the volume of peritoneal fluid to values approximately 300 per cent greater than those obtainable for nonpregnant animals of similar body weight is considerably above the expansion in plasma volume calculated from the data of Bond¹ to be only approximately 43 per cent greater on the twenty-first day of gestation than on the day of mating for the rat and only 48 per cent greater for pregnant women.² Although the elevation in blood volume during pregnancy in the rat is not apparent when calculated on the basis of the increase in body weight,5 this is certainly not true of peritoneal fluid, which was found to be increased preferentially. The possibility exists that the large amount of peritoneal fluid functions as a mechanical damper and as a buoyancy medium protecting the soft and gelatinous embryos from trauma due to sudden acceleration or deceleration and mechanical shock as well as from their own weight.*

in situ weight = weight in air
$$\left(1 - \frac{\text{density of peritoneal fluid}}{\text{density of organ}}\right)$$

= 59.6 grams $\left(1 - \frac{1.005}{1.047}\right)$
= 2.56 grams.

Similar values were obtained for the other animal tested. This effect would also prevent strain on the mesovarium and reduce similarly the weight of other viscera overlying the uterus. This effect would also prevent

^{*}For one animal, the uterus (including 14 embryos) weighed 59.6 grams. Archimedes' principle, the effective weight of the structure would be:

similar function has been ascribed to cerebrospinal fluid.¹⁴ In this connection, the density of peritoneal fluid found in this study is almost identical to that reported for cerebrospinal fluid, while density of uterine tissue is somewhat greater than the value reported for brain substance, as might be expected from the larger lipid content of the latter. The progressive increase in extracellular fluid (of which peritoneal fluid is a part) during pregnancy might be due to an increased production of certain of the water-retaining steroids by the adrenal cortex.

Peritoneal fluid is an excellent medium to study in vitro phagocytic activity quantitatively, especially toward physiological "particles." With the Randolph¹² diluent, eosinorrhexis¹⁵ is easily followed and the uptake by macrophages of degenerating eosinophils clearly evident, allowing the exact measurement of "active" macrophages and of "particles" phagocytized. The present finding of a greatly enhanced efficiency of phagocytosis in the course of the developing anemia of pregnancy is in accord with results of Berry and coworkers³-¹ indicating increased in vitro phagocytosis of bacteria by polymorphonuclear leukocytes in other types of anemias.

The anemia of pregnancy is evidenced early if measured in terms of hemoglobin or hematocrit values.¹ Plasma iron levels, however, remain normal at first even while erythrocyte values show their initial fall, but they descend precipitately during the latter stages of gestation in both man¹6-19 and the rat.²0 In our experiments, phagocytic activity paralleled more closely the lowered plasma iron levels than the erythrocyte parameters; phagocytosis was normal for animals on the tenth or fifteenth days of gestation and was found elevated only near the twentieth day of pregnancy. The increased phagocytic activity is especially significant since the cellular concentrations were materially reduced, an unfavorable factor as revealed by the studies of Hanks,²¹ showing that ''. . . increase in the absolute numbers of each component (numerical density of the system) causes higher phagocytic values and increasing action of the leukocytes on the bacteria per unit time. . . . ''

The fall in plasma iron during pregnancy may have practical value in affording resistance against infections. The enhanced leukocytic and reticulo-endothelial activity reported for other types of anemias³⁻⁷ also may be dependent on plasma iron levels. The relation of adrenal corticoids, known to be released in augmented amounts during pregnancy, to iron transport bears further study since the glucocorticoids have been stated to cause a fall in plasma iron levels.²² This might constitute a mechanism for the stimulation of phagocytosis reported in adrenalectomized rats receiving replacement treatment with adrenal hormones.²³

The advisability of routine dietary iron supplementation in human pregnancy requires re-evaluation in view of its apparent depressive effects on the reticuloendothelial system, especially when subacute infections are suspected. Similarly, procedures tending to reduce the extracellular water compartment,

nec. 1956

on,

hat

hat

ted

ra-

be

by

rtic

the

rore-

ent the

co-

oly-

of

nal end

t.20 red

mal ted rity reing ical ion

in ılodebe ars in ion eat-

egthe ted. ent,

such as excessive dietary salt restriction, may interfere with the buoyancy effect of the peritoneal fluid and cause undue tension on mesenteries supporting the genital tract.

Summary and Conclusions

Pregnancy in the rat results in an increase in volume of extracellular fluid which is disproportionately greater for the peritoneal space component. Macrophagic activity is stimulated in the advanced stages of gestation for rats on standard laboratory ration, but decreased in animals on iron-supplemented Although cellular concentrations in the peritoneal fluid are lowered during pregnancy, the absolute numbers of the various types of cells are elevated significantly because of the large increase in fluid volume. Calculations show that the peritoneal fluid during pregnancy may act as a buoyancy medium and mechanical damper for the protection of the genital tract.

References

- Bond, C. F.: Endocrinology 43: 180, 1948.
 Lund, C. J.: Am. J. Obst. & Gynec. 62: 947, 1951.
 Berry, L. J., Davis, J., and Spies, T. D.: J. Lab. & Clin. Med. 30: 910, 1945.
 Berry, L. J., Leyendecker, A. B., and Spies, T. D.: Blood, Spec. Issue No. 1, p. 98, 1947.
- Berry, L. J., and Haller, E. C.: Blood, Spec. Issue No. 1, p. 108, 1947.
 Berry, L. J., and Haller, E. C.: Blood, Spec. Issue No. 1, p. 117, 1947.
 Berry, L. J., and Spies, T. D.: Medicine 28: 239, 1949.

- Padawer, J., and Gordon, A. S.: Endocrinology 51: 52, 1952.
 Padawer, J., and Gordon, A. S.: J. Clin. Endocrinol. 13: 850, 1953.
 Padawer, J.: Doctorate Thesis, Graduate School of Arts and Science, New York Uni-10. Padawer, J.:

- Padawer, J.: Doctorate Thesis, Graduate School of Arts and Science, New York University, New York, N. Y., 1953.
 Gordon, A. S., and Padawer, J.: Federation Proc. 12: 54, 1953.
 Randolph, T. J.: J. Lab. & Clin. Med. 34: 1696, 1949.
 Snedecor, G. W.: Statistical Methods Applied to Experiments in Agriculture and Biology, Ames, Iowa, 1946, Iowa State College Press.
 Fulton, J. F., editor: Textbook of Physiology, ed. 16, Philadelphia, 1950, W. B. Saunders Company, p. 910.
 Padawer, J., and Gordon, A. S.: Blood 8: 388, 1953.
 Laurell, C. B.: Acta physiol. scandinav. 14: supp. 46, 1947.
 Laurell, C. B.: Pharmacol. Rev. 4: 371, 1952.
 Lundström, P.: Upsala läkaref, förh. 55: 1, 1950.

- 18. Lundström, P.: Upsala läkaref. förh. 55: 1, 1950.
- 19. Nylander, G.: Acta physiol. scandinav. 29: supp. 107, 1953.

- Nylander, G.: Acta physiol. scandinav. 25. supp. 107, 1933.
 Nylander, G.: Upsala läkaref. förh. 56: 11, 1951.
 Hanks, J. A.: J. Immunol. 38: 159, 1940.
 Cartwright, G. E., Gubler, C. J., Hamilton, L. D., Fellows, N. M., and Wintrobe, M. M.:

 In Mote, John R., editor: Proceedings of the Second Clinical ACTH Conference, Philadelphia, 1951, in Blakiston Company, vol. 1, p. 405.

 Gordon, A. S., and Katsh, G. F.: Ann. New York Acad. Sc. 52: 1, 1949.

THE UTERINE OMENTUM OF THE RAT AND ITS RESPONSE TO VASOCONSTRICTOR DRUGS*†

ROBERT LANDESMAN, M.D., AND BARBARA MENDELSOHN, A.B., NEW YORK, N. Y. (From the Department of Obstetrics and Gynecology, New York Hospital-Cornell Medical College)

FURTHER information has accumulated demonstrating that the finer peripheral circulation plays an active role in the changes of menstruation, pregnancy, and toxemia. Markee,¹ in a study of the anterior chamber of the eye, and Okkels,² in a histophysiological study, have shown the peripheral changes in the terminal vascular bed of the endometrium during the menstrual cycle. Variations in the peripheral circulation of the bulbar conjunctiva in normal pregnancy have been described.³ Other reports⁴⁻⁰ have illustrated the arteriolar constriction during toxemia in the retina, in the bulbar conjunctiva, and in the nail-bed vessels. The increased resistance in the cerebral circulation¹⁰ and the reduced blood flow in the kidneys in advanced toxemia¹¹ give indirect evidence of a disturbance in the peripheral vascular bed at these two sites. Although up to this time direct observation in vivo of the terminal vascular bed in the human uterus has not been possible, the studies just enumerated give us some indication of its importance.

Chambers and Zweifach¹² about ten years ago performed some limited unpublished work on the structural characteristics and reactivity of the vessels in the omentum contiguous to the rat's bicornuate uterus. This structure was easily exteriorized and the vasoconstrictor response of various drugs was tested on this vascular bed.

Anatomy

On either side of the bicornuate uterus of the rat is a fatty omentum which usually measures 4 cm. in length and is freely mobile. The blood vessels in these omental structures are a continuation of those supplying the uterine horns. In Fig. 1 these vessels may be seen in the lateral uterine horn and spreading into this omentum. By teasing out this fatty structure, it is possible in about 50 per cent of these animals to visualize clearly arteriolar, venular, and capillary circulations.

^{*}Purified oxytocin, synthetic oxytocin, and purified vasopressin were obtained from Dr. Vincent du Vigneaud, Department of Biochemistry, Cornell University Medical College, New York, N. Y.

Pitocin and Pitressin were obtained from Parke, Davis & Company, Detroit, Mich.

Methylergonovine tartrate (Methergine) and ergotamine tartrate (Gynergen) were obtained from Sandoz Pharmaceuticals, New York, N. Y.

Ergonovine maleate (ergonovine) was obtained from Burroughs Wellcome & Co. (U.S.A.) Inc., Tuckahoe, N. Y.

[†]This investigation was supported by grants from the United States Department of Health, Education and Welfare, National Heart Institute, H-1100 (C-3), and the James Foundation of the City of New York.

Technique

Mature rats of about 75 days old or older, weighing between 120 and 150 grams, were found to be most satisfactory. The rat is anesthetized by the intramuscular injection of about 3.5 mg. of sodium pentobarbital per 100 grams of body weight. The anesthesia is as light as possible so as not to affect the vascular bed. A vertical incision about one inch in length is made in the lower abdomen 0.5 cm. to the right or left of the midline. A special board was constructed for mounting the rat so that the uterine omentum might be exteriorized over a small transparent plastic chamber for direct microscopic observation. The animal is placed on this board lying on its side while the tubal omentum of that side is tested. The exteriorized tissue is bathed at 37° C. by a drip of Ringer's gelatin solution. The solution is maintained at this temperature by means of a thermoregulator. Fig. 2 shows this constant drip apparatus and rat board with an animal in working position. The source of illumination for the microscope is of low voltage to avoid excessive heat. The tissue of the omentum is brought out on the transparent plate by gentle manipulation with cotton applicators moistened with Ringer's gelatin solution. Any tugging or extra manipulation will result in an unsatisfactory preparation.

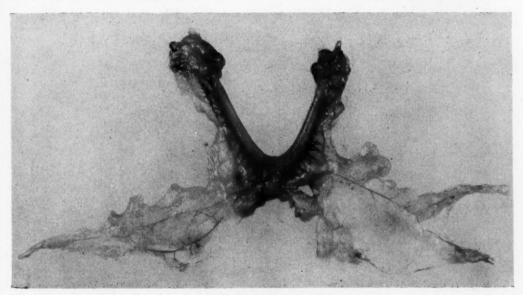


Fig. 1.

The ideal vessel is a medium-sized arteriole measuring approximately 15 microns. Surrounding capillaries and venules are also observed during the testing. Prior to the application of the various drugs, the reactivity of the vessel is demonstrated with diluted epinephrine. The usual range of normal vasoconstrictor response of the vessels is between 1:10 million and 1:50 million. If following the testing of any substance the epinephrine threshold changes, the preparation is discarded. In the presence of capillary thrombosis, diapedesis of leukocytes, or any other obvious variation in the vascular pattern, the animal is likewise sacrificed. The room is maintained at a constant temperature during the exposure of this tissue.

At the time of testing a pinchcock clamp is placed on the tubing which supplies the test tissue with Ringer's solution (Fig. 2). A tuberculin syringe with an 18 gauge needle is used for diluting the drug to the desired testing strength. Five drops of this material is topically applied to the tissue. When

a constriction is observed, the pinchcock clamp is removed from the tubing, thereby permitting the testing material to be washed off. A sufficient length of time is allowed between application of various drugs and different concentrations of the same drug. This permits the vessels to return to their normal physiological state for retesting. Fig. 3 shows the rat uterine omental

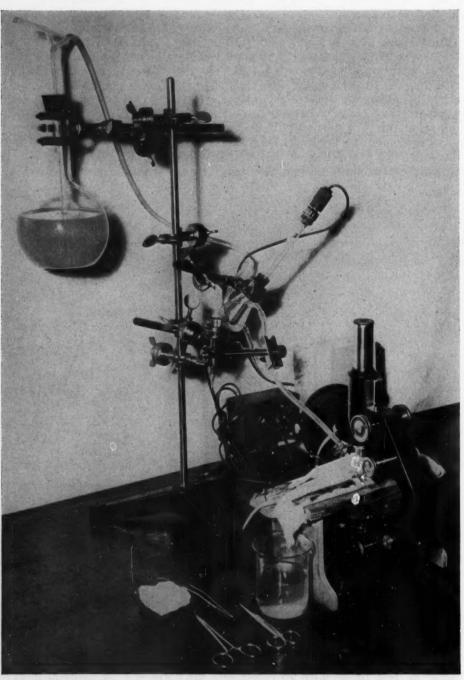


Fig. 2.

bed with a bifurcated large arteriole prior to topical application of epinephrine. Following contact with epinephrine hydrochloride, 1:50 million, there was obvious spasm of the arteriole, which is indicated by the arrow. This process was immediately reversible when the Ringer's gelatin solution washed away the epinephrine. A somewhat different process resulting in reduced blood flow and constriction is observed in the smaller arterioles. In Fig. 4 the arterioles are well filled. After epinephrine is applied there is complete emptying of the vessels and an absence of any blood column. Only the vessel walls themselves remain in the photograph. A larger accompanying venule demonstrates the granularity associated with reduced rate of blood flow. This process was also reversible.

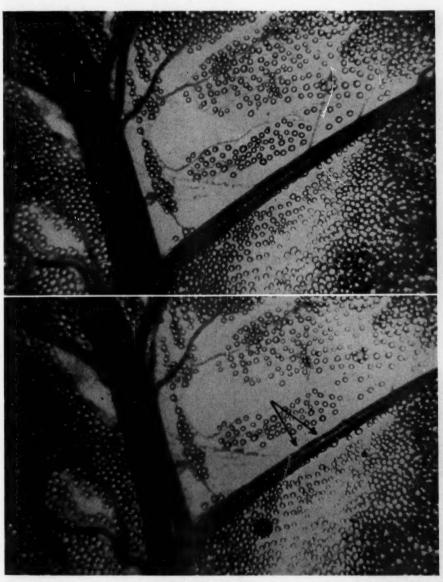


Fig. 3.—Rat uterine omentum: normal arteriole above and bulb spasm after epinephrine below.

Estrus Cycle

The first study was performed on fifty-seven animals to determine whether any differences in epinephrine sensitivity occurred during the various stages of the estrus cycle. Vaginal smears were taken of each animal in order to observe the cellular pattern. A uniform keratinization of vaginal epithelium and an absence of leukocytes are the characteristic findings in estrus.



Fig. 4.—Rat uterine omentum: normal arterioles above and emptying of arterioles after epinephrine below.

The presence of nucleated epithelial cells and polymorphonuclear leukocytes indicate metaestrus; diestrus smears show predominance of lymphoctyes, and proestrus shows nucleated epithelial cells alone (Table I). Various combinations and groupings were tried in an attempt to demonstrate differences in vascular sensitivity. The average for the various stages of the estrus cycle remained essentially the same and the response of 1:30 million was common to all phases.

TABLE I. ESTRUS CYCLE

			RINE DILUTION LION	
PHASE OF CYCLE	NO. OF ANIMALS	MAXIMUM DILUTION	MINIMUM DILUTION	AVERAGE DILUTION
Proestrus	7	1:50	1:8	1:22.7
Estrus	21	1:70	1:2	1:30.4
Metaestrus	16	1:70	1:8	1:27.4
Diestrus	5	1:30	1:20	1:25
Anestrus, unclassified	8	1:50	1:10	1:30

Pituitary Substances

A. Oxytocin.—Table II lists the data on the peripheral vascular response to various fractions of posterior pituitary extract. The highly purified natural oxytocin,13 free of vasopressin, and a sample of synthetic oxytocin14 were employed. A stock solution of 0.1 I.U. per cubic centimeter was used for the commercial Pitocin, whereas with the purified or synthetic oxytocin higher concentrations of 3 and 4 units per cubic centimeter were applied. These substances were compared both in the same animal and in different animals. Epinephrine was again used to standardize the vascular bed before each testing. If there were any differences in the constrictor response of epinephrine after the testing of a drug, the preparation was discarded and the result was not included. The data are all standardized in international units per cubic centimeter. All test animals showed greater vasoconstrictor activity from topically administered commercial Pitocin than from the purified and synthetic oxytocin. The Pitocin constrictor response was tenfold that of the more purified and synthetic oxytocin. There was some vasoconstrictor response in the more purified forms, but this was minimal.

TABLE II. POSTERIOR PITUITARY SUBSTANCES

COMPOUND	NO. OF	RESPONSE A DILUT CONCENTE (I. U.	E ATION	RESPON MAXII CONCENT (I. U	MUM RATION	AVERAGE
Pitocin, commercial	25	.01	2+	.1	+	.054
Oxytocin, purified	25	.1	2+	4.0	3+	.9
Oxytocin, synthetic	10	.1	2+	3.0	2+	1.2
Pitressin, commercial	25	.0001	2+	.1	+	.0081
Vasopressin, purified arginine	20	.00001	3+	.005	3+	.00154

B. Vasopressin.—Highly purified arginine vasopressin^{15, 16} and Pitressin were compared in the same and different rats. The Pitressin contained 20 pressor units per cubic centimeter. The purified vasopressin consisted of 10 to 20 pressor units per cubic centimeter.

The rat omental vascular preparation was highly sensitive to these pressor substances as indicated by Table II. The purified vasopressin is very high in vasoconstrictor activity, and demonstrates six times more vasoconstrictor material than the commercial preparation unit for unit.

Ergots.—A comparison was made among the three different ergot preparations to show their relative vasoconstrictor response on this vascular bed (Table III). In almost every animal the tests were uniform. Methylergonovine tartrate (Methergine) showed no vasoconstrictor response in 87 per cent of the animals at full strength (0.2 mg. per cubic centimeter). Ergonovine maleate (ergonovine) was intermediary among the three compounds in its effect; one-half of the animals tested showed a positive response at maximum con-

centration. Ergotamine tartrate (Gynergen) required the greatest dilution to obtain the threshold response, and among these three compounds showed the highest tonic activity.

TABLE III. ERGOT COMPOUNDS

COMPOUND	NO. OF ANIMALS	MAXIMUM DILUTION FOR REACTIVITY	NUMBER WITH NO REACTION
Methylergonovine tartrate	17	.01 mg./c.c. 2+	14
Ergonovine maleate	17	,005 2+	3
Ergotamine tartrate	11	.0005 2+	0

Comment

Up to the present time no satisfactory direct method has been devised for the study of the peripheral vascular bed in the reproductive tract of women. Transplantation of endometrium to the anterior chamber of the eye has provided valuable information concerning vascular alterations during the menstrual cycle of the monkey. Indirect evidence indicating generalized vascular variations has accumulated for the menstrual cycle and normal and toxemic pregnancy. Vessel alterations in the peripheral flow pattern have been observed in the bulbar conjunctiva during the normal menstrual period, normal pregnancy, and the toxemias. In the nail bed, constriction of the arteriovenous network has been repeatedly observed during acute toxemia. Diminished renal blood flow is reported in the more severe forms of this disease. Sheehan¹⁷ has demonstrated arteriolar constriction of the kidney in pathological specimens from patients with acute eclampsia. McCall,¹⁰ while studying the cerebral circulation, has shown an increase in peripheral vascular tone and reduced blood flow in eclampsia.

The uterine omentum of the rat contains the same blood vessels that supply the uterine horns. By exteriorizing this tissue, direct microscopic observations and reactions to drugs were made available. Initial studies to determine if any variations occurred in this vascular pattern in the estrus cycle were uniformly negative as indicated by Table I. The average dilution for a constrictor response with epinephrine, in a total of 57 animals satisfactorily tested, was 1:30 million. Since no significant variation of this response due to period of cycle was observed, the vascular bed was considered suitable for testing the vasoconstrictor activity of various drugs without regard to the stage of estrus.

Because of the recent extensive use of commercially available Pitocin for the induction and stimulation of labor, and the importance of possible vaso-constriction produced by any posterior pituitary substance, a detailed investigation of this hormone's reactivity on the rat uterine omentum was undertaken. In this study, new recently purified oxytocic preparations were used. The purified and the synthetic oxytocins were tested along with the commercial Pitocin. In all test animals Pitocin contained more vasoconstrictor factor than did the purified natural or synthetic oxytocin.

In the recent four-year period from 1951 to 1954 in this clinic, there were 433 patients with severe toxemia of pregnancy. Twenty-nine were delivered by means of induction with Pitocin. There were 5 fetal deaths in this group

with induced labor. One of the infants in the immature group died during the induction. In the remaining 4 patients, the fetal heart sounds disappeared prior to the use of Pitocin. A review of toxemia patients in this clinic who had Pitocin stimulation or induction failed to indicate any true vasopressor effect associated with concentrations used for this therapy. Although one fetal death was associated with the direct administration of Pitocin, no pressor effect was noted at the time. After a careful review of the clinical data, this death could not be attributed to the use of Pitocin. Certain reports in the literature indicate that on occasion Pitocin may result in a severe sudden pressor effect and fetal death. Milton,18 in discussing the presentation of Mauzy and Donnelly, reports that one patient with essential hypertension, given 1 minim of Pitocin intravenously, had rises in blood pressure up to 200/120; four days later ½ minim likewise resulted in a blood pressure elevation as high as 200/150. Although the peripheral blood pressure may show no variation with Pitocin, it is quite possible that a constrictor effect may be produced in the uterine vascular bed. Since a highly purified natural oxytocin free of vasopressin shows a lower vasoconstrictor effect on the uterine omental vessels, it may well be the safer agent for clinical use.

A preliminary comparative study of commercial Pitressin and purified vasopressin isolated from the beef pituitary indicated the consistently higher vasoconstrictor activity of the latter. This purified vasopressin gave a positive vasoconstrictor response on our test vascular tissue at a dilution of 0.00001 I.U. per cubic centimeter. Further evaluation of this vasopressor activity is necessary.

Recently much has been written concerning the vasoconstrictor activity of ergot compounds frequently used in the third stage of labor. Studies by Schade, Hamilton, Priver, and Murphy have all shown that methylergonovine tartrate has a lowered vasopressor response as compared to ergonovine maleate. Besides these two ergot preparations, a known vasoconstrictor, ergotamine tartrate, was used in this study on the uterine omentum. Topical tests showed conclusively that methylergonovine tartrate has the least vasoconstrictor effect on this vascular preparation and ergotamine tartrate has the most effect. These direct observations on vessels of the reproductive tract further support the opinions already presented in the clinical literature indicating the minimal vasoconstrictor response associated with methylergonovine tartrate. The topical constrictor response of this drug is less than that of commercial Pitocin in our particular study. A preliminary study of methylergonovine tartrate during labor shows no toxic vascular effects.²³

Because of obvious technical difficulties, it has not been possible to study the peripheral circulation in the human female genital tract in vivo. The importance of the specific vessel alterations has been indicated by the variations demonstrated in the vascular bed in more available external areas during menstruation, pregnancy, and toxemia of pregnancy. In this study the vascular bed of the uterine omentum of the rat was observed and studied in vivo without undue difficulty for periods of time up to one to two hours. With

the use of this tissue, under a standard technique, the vasoconstrictor responses of two important pharmacological agents, posterior pituitary fractions and the ergotrates, have been elaborated.

Conclusions

- 1. A satisfactory technique is described for the study of the peripheral vascular bed in the uterine omentum of the rat.
- 2. The effect of various drugs was determined by topical administration in serial dilutions.
- 3. Epinephrine sensitivity remains stable for a period of one to two hours and varies between 1:50 million and 1:10 million.
- 4. No difference in vascular response was noted in the various stages of the rat estrus cycle.
- 5. Commercial Pitocin demonstrates a tenfold higher constrictor response than isolated natural oxytocin or synthetic oxytocin.
- 6. Some minimal vasoconstrictor effect is demonstrable by this technique with synthetic and purified oxytocin.
- 7. This evidence suggests that the pure and synthetic forms of oxytocin may be more satisfactory for clinical use because of their reduced vasoconstrictor action.
- 8. Pure vasopressin shows a higher vasoconstrictor effect than commercial Pitressin.
- 9. Methylergonovine tartrate has the least vasoconstrictor effect of the three ergot compounds and is most suited for obstetrical use because of this minimal activity.

References

- Markee, J. E.: In Engle, Earl T., editor: Menstruation and Its Disorders, Springfield, Ill., 1950, Charles C Thomas, Publisher, p. 165.
 Okkels, H.: In Engle, Earl T., editor: Menstruation and Its Disorders, Springfield, Ill., 1950, Charles C Thomas, Publisher, p. 139.
 Landesman, R., Douglas, R. G., Dreishpoon, G., and Lee, R. E.: Am. J. Obst. & Gynec.
- 65: 876, 1953.
 4. Hallum, A. V.: J. A. M. A. 106: 1649, 1936; South. M. J. 31: 64, 1938; Arch. Ophth. 37: 472, 1947.
 5. Landesman, R., Douglas, R. G., and Snyder, S. S.: Am. J. Obst. & Gynec. 62: 1020,
- 1951.
- Landesman, R., Douglas, R. G., and Holze, E.: Am. J. Obst. & Gynec. 68: 170, 1954.
- Hinselmann, H., Nettekoven, H., and Silberbach, W.: Arch. Gynäk. 116: 443, 1922.
 Mufson, I.: Am. J. Obst. & Gynec. 15: 800, 1928.

- Murson, I.: AM. J. Obst. & Gynec. 15: 800, 1928.
 Nevermann, H.: Zentral. Gynäk. 45: 609, 1921.
 McCall, M. L.: Surg., Gynec. & Obst. 89: 715, 1949.
 Assali, N. S., Kaplan, S. A., Foman, S. J., Douglas, R. A., Jr., and Suyemoto, R.: J. Clin. Invest. 32: 44, 1953.
 Chambers, R., and Zweifach, B.: Unpublished work.
 du Vigneaud, V., Ressler, C., Swan, J. M., Roberts, C. W., and Katsoyannis, P. G.: J. Am. Chem. Soc. 76: 3115, 1954.
 Pierce, J. G. Gordon, S. and du Vigneaud, V.: J. Biol. Chem. 199: 929, 1952.

- Pierce, J. G., Gordon, S., and du Vigneaud, V.: J. Biol. Chem. 199: 929, 1952.
 Turner, R. A., Pierce, J. G., and du Vigneaud, V.: J. Biol. Chem. 191: 21, 1951.
 Popenoe, E. A., Pierce, J. G., and du Vigneaud, V.: Proc. Soc. Exper. Biol. & Med. 81: 506, 1952.
- 17. Sheehan, H. L.: Brit. M. J. 2: 1327, 1950.
- Milton, John D.: Discussion of Mauzy, C. H., and Donnelly, J. F.: Am. J. Obst. & Gynec. 64: 517, 1952.

- 19. Schade, F. F., and Gernand, H. C.: Am. J. Obst. & Gynec. 59: 627, 1950.
 20. Hamilton, H. G., Higgins, R. S., and Alsop, W. S., Jr.: South. M. J. 45: 728, 1952.
 21. Priver, M. S., Harris, J. M., Krohn, L., and Boros, H. H.: West. J. Surg. 57: 586, 1949.
 22. Murphy, H. S.: Am. J. Obst. & Gynec. 64: 419, 1952.
 23. Property J. C.: App. West. Mod. & Surg. 4: 23, 1950.
- 23. Brougher, J. C.: Ann. West. Med. & Surg. 4: 33, 1950.

PREGNANCY COMPLICATED BY AMYOTROPHIC LATERAL SCLEROSIS

J. Wilson Huston, Commander (MC) USN,* John Lingenfelder, M.D., Corpus Christi, Texas, and Donald W. Mulder, M.D.,** and Leonard T. Kurland, M.D.,*** Rochester, Minn.

(From the Department of Obstetrics and Gynecology, Guam Naval Hospital)

MYOTROPHIC lateral sclerosis occurs on the island of Guam and other Marianas Islands in an estimated frequency of 100 times that of the disease in the continental United States of America. This unexplained concentration of a rare disorder on a small and distant island chain has been the subject of an intensive investigation by clinicians, pathologists, epidemiologists, and geneticists, and the inquiry is still under way. The present paper deals with an investigation on the effects of pregnancy, labor, and parturition on amyotrophic lateral sclerosis, and the effect of amyotrophic lateral sclerosis on pregnancy and the newborn. It has been reported that the amyotrophic lateral sclerosis observed on Guam and the other Marianas Islands is clinically and pathologically a classic form of the disease. This illness has been recognized as highly prevalent on Guam for at least 100 years. Although the cause of this disease has not been established, the disorder on Guam is believed to be an unusual inherited form of the disease.^{1, 2, 3}

Guam is the largest of the Marianas Islands in the western Pacific. It lies about 13 degrees above the Equator. It is approximately 1,500 miles south of Japan and 1,500 miles east of the Philippine Islands. The natives of Guam, or Chamorros, are of mixed racial origin. It is thought that they originally came from southeastern Asia, and that an intermixture with Filipino and Spanish soldiers occurred after the Spanish conquest of Guam.¹

Definition of the Syndrome

Amyotrophic lateral sclerosis is a neurological disorder of unknown cause which occurs in adult persons. It is invariably fatal; there is no recognized therapy. In the past, progressive muscular atrophy and progressive bulbar palsy were considered to be separate clinical entities, but today most authorities on neurology consider them as clinical components of the symptom complex of amyotrophic lateral sclerosis.

Pathologically, the disorder is characterized by progressive degeneration and loss of cells of the anterior horn of the spinal cord and motor nuclei of the

^{*}Department of Obstetrics and Gynecology, United States Naval Hospital, Beaufort, S. C. **Section of Neurology, Mayo Clinic.

^{***}Chief, Epidemiology Branch, National Institute of Neurological Diseases and Blindness, Public Health Service, Department of Health, Education and Welfare; Research Associate, Mayo Clinic and Mayo Foundation.

brain stem, and demyelination of the lateral columns, particularly of the pyramidal tracts of the spinal cord and, rarely, of the medulla. Degeneration of the Betz cells also has been described.

Clinically, in progressive muscular atrophy, muscle fasciculations, weakness, and atrophy occur at any or all spinal levels. In most cases the intrinsic muscles of the hands and shoulder girdle are involved first. The disorder usually begins on one side, and shortly thereafter the other side likewise may be involved. Changes in the lateral columns, which are found at necropsy in most cases of progressive muscular atrophy, may be masked clinically by the severe muscle atrophy.

Progressive bulbar palsy indicates similar motor neuronal degeneration at the level of the medulla and pons. Weakness, atrophy, and fasciculations of the muscles of the tongue, pharynx, larynx, jaw, and face develop, with progressive dysphagia and dysarthria. Because the duration from onset to death usually is shortest in this latter form, clinical signs of upper motor neuron disease often may fail to develop.

Amyotrophic lateral sclerosis is the form of progressive motor neuron disease which is most often seen. In addition to progressive muscular atrophy or progressive bulbar palsy, involvement of the corticospinal or the corticobulbar tract is prominent. The signs of upper motor neuron changes at the spinal levels are referred to as "lateral sclerosis"; at the bulbar level, they are referred to as "pseudobulbar palsy." Other characteristic features of amyotrophic lateral sclerosis are the absence of sensory abnormalities, primary incoordination, or mental impairment, and the persistence of the abdominal reflex and the control of bowel and bladder sphineters.

Review of Literature

The extremely low prevalence of amyotrophic lateral sclerosis (4 per 100,000 persons, except in the Marianas Islands), the lower incidence among females, and the preponderance of persons attacked when they are past the age of reproduction in all probability account for the very few cases of pregnancy in amyotrophic lateral sclerosis reported in the world's medical literature. The 6 cases which we were able to locate will be reviewed.

Lignitz,⁴ in Germany, described a case in which amyotrophic lateral sclerosis attacked a 23-year-old woman who had had three normal deliveries. During her third pregnancy she noted the gradual onset of a spastic gait, and weakness and wasting of the right hand and shoulder. Delivery was uncomplicated, and a few months later she again became pregnant. On examination at 3 to 4 months of pregnancy, findings consistent with the diagnosis of amyotrophic lateral sclerosis were noted. It was considered advisable to terminate the pregnancy; however, the progressive course of the disease was not affected during the brief follow-up after the pregnancy had been interrupted. According to Lignitz, Probst⁵ described 3 cases, in a series of 28 cases of amyotrophic lateral sclerosis, in which the illness had occurred during pregnancy. None of the pregnancies were interrupted and no attempt was made by Probst to show any cause or relationship of the amyotrophic lateral sclerosis to the pregnancy.

Murphy⁶ in New York City reported one case of amyotrophic lateral sclerosis in which pregnancy occurred. The patient, a 39-year-old housewife, had had 9 full-term pregnancies, all followed by spontaneous delivery. The tenth pregnancy occurred about 6 years after the onset of slow, progressive amyotrophic lateral sclerosis. At the time of the examination, the patient had severe dysarthria and dysphagia, exaggerated reflexes, and marked muscular atrophy in all four extremities. After 2 hours of labor she was delivered of a healthy 8 pound baby. There was only the usual loss of blood and the postpartum course was normal. The patient died 2½ years later. Murphy concluded that the disease does not affect the reproductive organs and has no effect on pregnancy. He recommended that pregnancy be allowed to continue to term, and he said that a good result could be expected.

Cazzola⁷ in Italy reported a condition diagnosed as amyotrophic lateral sclerosis in which pregnancy occurred about a year after the onset of symptoms. The pregnancy was allowed to go to term, since it was felt the course of the disease would not be affected by its interruption. The symptoms described in this paper do not fit the classic picture of amyotrophic lateral sclerosis.

Method of Study

The unusually high concentration of patients with amyotrophic lateral sclerosis on the island of Guam and the high birth rate on the island gave us an unusual opportunity to study the relationship of pregnancy to the disease in question. Two of us (Huston and Lingenfelder), while stationed at the Guam Naval Hospital, were charged with delivering the infants of 5 patients in this hospital who had amyotrophic lateral sclerosis. Additional data were obtained from patients whose infants had been delivered at home while the patients had this disease. In most instances, accurate information concerning the actual delivery of infants among these patients could not be obtained, except for the report from the midwife and patient that these had appeared normal. In every case, however, it was possible to carry out a complete neurological study. In 10 cases such study was conducted by us and in 7 additional cases it was conducted by Drs. Koerner or Arnold. Additional data on the children born of these women have been obtained in follow-up studies which were conducted as late as January of 1955.

Data

During the course of this study 17 women with amyotrophic lateral sclerosis were delivered of a total of 21 infants (Table I). Eleven of these mothers have since died and postmortem studies in 2 cases have verified this diagnosis. Four of the patients were 30 years old or less, 6 were from 31 to 40 years of age, and 9 were 40 years of age or older at the time of delivery. The unusual incidence according to age is in part a reflection of the average age of the patient at the onset of amyotrophic lateral sclerosis, but also demonstrates the frequency with which women on the island of Guam have children at an advanced age.

There was no specific effect of the pregnancy on the course of this disease, and the pregnancy did not seem to be altered in any specific way by the disease. In no instance was the patient improved by the pregnancy. Amyotrophic lateral sclerosis is a progressive disease, from which death occurs, on an average, within 3 years. A number of our patients with amyotrophic lateral sclerosis became

pregnant late in the course of their disease, and died prior to delivery. These have not been included in this series. One of our patients was pregnant twice during the course of her illness; she was delivered of a normal baby on the first occasion, but she died during the fourth month of the second pregnancy.

In those patients in whom the natural course of the neurological disease was such that they survived to term, the added stress of the pregnancy often proved most difficult. Motor function already severely impaired by the illness frequently became inadequate, and many patients became bedfast during their pregnancy. The terminal severe disability in swallowing and breathing made it difficult for the patient to obtain adequate nutrition and oxygen.

TABLE I. SALIENT DATA CONCERNING 17 PATIENTS WHOSE PREGNANCY WAS COMPLICATED BY AMYOTROPHIC LATERAL SCLEROSIS

PATIENT	NO. OF PREVIOUS PREGNAN- CIES	NO. OF PREGNAN- CIES DURING ILLNESS	AGE AT TIME OF DELIVERY*	DURATION OF ALS AT TIME OF DELIVERY (YEARS)	STATUS OF INFANT	PRESENT STATUS OR AGE OF PATIENT AT DEATH
1	5	1	46	1	Normal	Dead, 51
2	12	1	43	1	Normal	Dead, 48
3	11	2	45 and 46	1 and 2	Normal	Dead, 50
4	7	1	41	2	Normal	Dead, 42
5	4	2	31 and 32	1 and 2	Normal	Living, 37
6	1	1	20	1	Normal	Living, 23
7†	7	1	37	3	Normal	Dead, 38
8	1	1	40	2	Normal	Dead, 41
9†	1	1	39	2	Normal	Living, 41
10	9	1	39	2	Normal	Living, 41
11	9	1	37	3	Harelip, cleft palate	Dead, 37
12	5	3	29, 30, 31	1, 2, 3	Normal	Living, 32
13	10	1	45	1	Normal	Dead, 48
14	4	1	44	1	Normal	Dead, 48
15	15	1	42	1	Normal	Living, 44
16	5	1	30	1	Normal	Dead, 31
17	4	1	41	3	Anencephalic monster	Dead, 42

*More than one age is given because 21 infants were born to the 17 patients as individual births.

†Presented also in the text of this paper.

If, in spite of the progression of the illness, the patient survived, delivery was normal. This was true even when muscular atrophy and weakness were profound. Apparently, in none of these patients was the smooth musculature of the uterus involved, although frequently the perineal muscles were markedly atrophied. All these patients were multiparous, and, as might be expected, this in itself aided in the ease of delivery.

Of the 21 children who were born to these 17 women, 19 appeared normal at birth and have remained so to the date of this report. Two of these chil-

dren had severe congenital anomalies. The mother of one of these infants was 41 years old at the time of the birth of her child, which was an anencephalic monster. The second mother was 37 years old at the birth of her child, who had a cleft palate and harelip.

Two representative cases will be presented next.

Report of Cases

Case 1.—A 37-year-old Guamanian native was first examined at the Guam Naval Hospital in February, 1948. The neurological examination by Dr. Koerner revealed marked muscular atrophy and fasciculations in the upper extremities, with less atrophy and some rigidity in the lower extremities. Fasciculations in the tongue were noted, and the patient had dysarthria and dysphagia. All the deep reflexes were hyperactive and Babinski signs were present on each side. No sensory abnormalities were elicited. Results of the general physical examination were negative, and those of routine laboratory procedures were within normal limits (Kahn test, blood counts, urinalysis). Examination of the cerebrospinal fluid showed normal pressure, 4 cells per cubic millimeter, a negative reaction to the Wassermann test, and a protein content of 30 mg. per 100 c.c. The patient had completed seven pregnancies without complications and had been delivered of seven normal children.

On Jan. 19, 1950, she was admitted to the United States Naval Hospital with a diagnosis of "threatened premature labor" as a result of a fall from bed at home. The diagnosis of pyelonephritis was made, and, with treatment, symptoms subsided. She was readmitted on April 20, 1950, complaining chiefly of intermittent abdominal contractions. These subsided after rest in bed and sedation. On May 24, 1950, the patient was admitted in labor, and shortly thereafter was delivered of a normal, viable female infant weighing 5 pounds and 14 ounces, by left occiput posterior presentation, with the aid of low forceps. The postpartum course was normal, and the patient was discharged on the sixth postpartum day.

The patient was seen at home 6 months later. It was observed that the child was progressing normally, and was being taken care of by relatives. The patient died in May of 1951. The child was examined in January of 1955, at which time she appeared normal.

Case 2.—A 39-year-old Guamanian woman originally was examined in December of 1953, at which time she was 6 months pregnant. The patient said that several months prior to our examination she had noted the onset of difficulty in swallowing and talking. More recently, she had noted weakness in the arms. Examination showed bilaterally hyperactive deep reflexes, including the jaw jerk. The Babinski sign was present bilaterally. Examination of the tongue disclosed weakness, atrophy, and fasciculations bilaterally. Examination of the upper extremities demonstrated minimal weakness and atrophy.

On April 30, 1954, this patient was admitted to the United States Naval Hospital in early labor. She was at term; the prenatal course had been entirely normal. She was delivered of a normal infant spontaneously, by left occiput anterior presentation. Trichloroethylene was used for analgesia and anesthesia. The third stage of labor was normal.

On June 17, 1954, re-examination showed nothing abnormal from an obstetric standpoint. The symptoms of amyotrophic lateral sclerosis had progressed.

The patient was re-examined in September of 1954. Her condition had deteriorated steadily and progressively since her previous neurological examination in November of 1953. Examination again disclosed hyperactive reflexes, with Babinski signs and sucking reflexes. The atrophy and weakness of the tongue had progressed, and at this time the patient had considerable difficulty in swallowing. Examination of the musculature of the extremities showed atrophy and weakness, most prominent in the interossei muscles. The patient walked with difficulty.

Re-examination of this patient in January of 1955 showed that progression of all signs and symptoms had occurred. She no longer was able to walk or to speak intelligibly. The child born in April of 1954 appeared normal.

Comment

In these 17 patients whom we had the opportunity of studying on the island of Guam, pregnancy did not alter the course of the disease. Pregnancy, when it did occur, and when the course of the disease was such that the patient lived sufficiently long, appeared normal. Delivery was usually spontaneous and uneventful in these multiparous patients. The infants in all but 2 instances were normal, and have shown a normal development. The abnormalities of the 2 fetuses did not seem to be the results of a specific reaction to the amyotrophic lateral sclerosis. It is possible that they were related to the age of the mothers and to the secondary effects of amyotrophic lateral sclerosis, such as poor nutrition and hypoxia, which so often accompany this disease. The absence of accelerations or remissions in the course of amyotrophic lateral sclerosis during pregnancy and the successful carrying to term of a normal pregnancy in the majority of these patients might possibly suggest that endocrine factors are not important etiologically in the disease, or are not commonly associated with amyotrophic lateral sclerosis.

Although pregnancy appears to have no direct influence upon the course of the disease, it creates many special problems for the patient who has amyotrophic lateral sclerosis and for the obstetrician earing for her. The impairment of muscular strength makes it difficult for the patient with even moderate involvement to care for herself. Unfortunately, as the pregnancy progresses, the amyotrophic lateral sclerosis can be expected to become progressively more severe. Thus, it is important to advise the patient to avoid excessive fatigue and to arrange for adequate help both for herself and, following delivery, for the baby.

The most serious complications of the disease are secondary to the paralysis of the facial, oral, and laryngeal musculature, with resultant inability to obtain adequate fluids and foods orally, as well as the additional danger of complicating aspiration pneumonia. For some patients it may become necessary to rely on nasal gavage or gastrotomy to maintain adequate nutrition. An interested and sympathetic relative, however, who is willing to spend the necessary time to feed the patient, may be able to maintain an adequate fluid and caloric intake.

The progressive paralysis of the intercostal and diaphragm muscles, with the pregnancy and aspiration pneumonia, if it occurs, may so diminish the respiratory exchange as to create severe anoxia. An adequate airway in these patients may be difficult to maintain because of the patient's inability to handle secretions in the throat. Frequent aspiration or even tracheotomy may become necessary. Oxygen administered by tent or tube is often indicated. In certain instances a respirator may become essential to maintain the life of the patient in the last several weeks of the pregnancy.

Delivery itself usually creates no special problems. The smooth musculature of the uterus is not involved, and the musculature of the perineal floor usually is so atrophic as to create no impediment to delivery.

The patient who has amyotrophic lateral sclerosis, although suffering from a progressive neurological disease, is mentally alert. Although the motor in-

f

1

1

e 2

C

S

3

e

t.

f

C f

volvement may be severe, there is no associated sensory disturbance or dysfunction of the bladder. Unfortunately, it can be predicted that the mother with amyotrophic lateral sclerosis will not be able to care for her child through its infancy. It is almost certain that she will be dead before the child is 3 years of age. Thus, it becomes necessary for the obstetrician to assist the family and the patient in preparing for this inevitable course of events.

Summary and Conclusions

The effect of pregnancy on amyotrophic lateral sclerosis and the effect of amyotrophic lateral sclerosis on pregnancy and delivery were studied in 17 patients on the island of Guam. The progressive nature of the amyotrophic lateral sclerosis is not altered by the pregnancy, except when the disease is far advanced, in which event an enlarged uterus may add to respiratory dysfunction. Patients with amyotrophic lateral sclerosis who become pregnant are able, in most instances, to be delivered of normal infants. They frequently need special care, however, because of the problems peculiar to this disease.

References

- Mulder, D. W., and Kurland, L. T.: Proc. Staff Meet., Mayo Clin. 29: 666, 1954.
 Arnold, Arthur, Edgren, D. C., and Palladino, V. S.: J. Nerv. & Ment. Dis. 117: 135, 1953.
 Koerner, D. R.: Ann. Int. Med. 37: 1204, 1952.
 Lignitz, Wilhelm: Ein Fall von Graviditat bei amyotrophischer Lateralsklerose, Thesis, Leipzig, 1920, Druck von G. Kreysing.
 Probst, M.: Quoted by Lignitz, Wilhelm.⁴
 Murphy, A. J.: Am. J. Obst. & Gynec. 18: 845, 1929.
 Cazzola, Dino: Ann. ostet. e ginec. 71: 501, 1949.

TREATMENT OF CANCER OF THE CERVIX UTERI*

Professor M. A. van Bouwdijk Bastiaanse,** Amsterdam, Holland

UP TO 1940 the number of gynecologists employing surgical treatment was very small. This has, however, been changed by the considerable stimulus received from the United States of America. I believe that I should mention Meigs as having been chiefly responsible for this change. Primary mortality from Wertheim's operation, which, about twenty years ago, still was approximately 10 to 15 per cent, has now declined, being in good hands, to under 1 per cent (Table I).

TABLE I

AUTHOR	YEAR	PER CENT
Wertheim ¹	1910	33.0
	1907-1936	14.0
Bonney ²	1936-about 1950	11.0
	Prior to 1948	7.4
Pratt ³ (Mayo Clinic)	1948-1950	0.0
Meigs4		0.0
van Bouwdijk Bastiaanse		0.0

The course of primary mortality in Schauta's operation is shown in Table II.

TABLE II

AUTHOR	YEAR	PER CENT
Schauta ⁵	1901-1905	11.4
	1906-1911	6.4
	1912-1916	4.3
	1917-1920	3.5
Stoeckel ⁶	1928	4.8
Mitra7		2.8
In last 105 cases		0.0
van Bouwdijk Bastiaanse	1927-1938	4.0
•	1939-1954	1.3
	(Not including 2	war casualties)
	1942-1954	0.2
	(Not including 2	war casualties)
No primary mortal	lity in last 315 operations	,

To determine the best method of treatment, the following questions should be answered:

- 1. What is the primary death rate?
- 2. What is the rate of permanent recovery?
- 3. Can severe damage occur as a result of treatment?

^{*}Presented at a meeting of the Chicago Gynecological Society, Dec. 17, 1954.

^{**}Head of the Department of Obstetrics and Gynecology, University of Amsterdam.

us

ity xiler

ble

uld

The results obtained can be compared only when complete information about the patients who have reported to the hospital is stated. This includes the number of patients of the various groups, the various methods of treatment, with a statement of their differences and the results obtained with each method as well as in the total number of patients. Unfortunately, a large number of recent papers has failed to meet these requirements. Frequently only the division into groups of the surgical patients is stated. Table III shows the considerable extent to which the number of operations performed may vary.

TABLE III

AUTHOR	YEAR	PER CENT
Corscaden ⁸	1951 for the U.S.A.	10-15
Meigs4	1939-1940	15.0
Has continually increased sinc	e 1946, now approximately	60.0
Anderes9	1941-1946	24.0
	1946	26.0
Stoeckel ⁹	1931-1937	33.0
Navratil ¹⁰	1947-1953	41.5
Bonney ⁹	1907-1936	63.0
Amreich ¹¹	1939-1943	74.0
van Bouwdijk Bastiaanse	1939-1950	55.0
•	1952-1954	70.0

On the whole it may be stated that the smaller the number of surgical cases, the less extensive the carcinomas and the greater the number of untreated patients who are poor operative risks. When the number of operations was limited to about 10 per cent some thirty to forty years ago, recovery rates of 80 to 85 per cent were also obtained.

The division into groups also is insufficient to permit a comparison, as personal views will play an important part in this classification. At the Congress of German Gynecologists¹² held in 1941 it appeared that the groups showed marked variations in size, which could be attributed only to a difference in appraisal of the investigator. To gain an insight into the significance of personal evaluation, Heyman and Kottmeyer¹³ independently divided the patients into groups. A difference was observed in only 10 per cent of the cases. Heyman and Kottmeyer belong to the same school. Investigations into the role of personal factors would be much more valuable if the division were made by two persons from different schools who are not attached to the hospital where the investigation is carried out. For the time being, however, there is no better method by which to make comparisons than that of dividing the patients into groups. Especially with regard to the significance of the personal factor, I believe a complete statement concerning all the patients who have reported to the hospital to be essential.

Another important factor in forming an opinion on the data reported in the literature is that, contrary to internationally established rules, the group in which the patient was included prior to treatment occasionally is changed after operation. The change will almost always be to a poorer group, on account of the finding of positive lymph nodes or the degree of spread. This fact rules out any comparison with the results of radium therapy.

Mortality

Primary Death Rate.—Primary mortality in all methods of treatment has declined to a negligible proportion (Tables I, II, and III).

TABLE IV. PRIMARY MORTALITY FOLLOWING TREATMENT WITH RADIUM

AUTHOR	YEAR	PER CENT
van Rooy14	1923-1938	5.3
Eymer ¹⁵ for various investigators		1.3-5.5
van Bouwdijk Bastiaanse	1939-1954	2.0
	(7 out of 358)	
No deaths after 1947	(, , , , , , , , , , , , , , , , , , ,	

Permanent Recovery.—Permanent results will depend upon local recurrences or metastases. Local recurrences following radium therapy may be due to one of the following causes: (1) resistance to radium irradiation, (2) the fact that some of the cancer cells are too far removed from the radium source to be destroyed, or (3) the appearance of another carcinoma in the remaining cervix, in which the first carcinoma also developed.

TABLE V. LOCAL RECURRENCES FOLLOWING TREATMENT WITH RADIUM

		PER CENT
	van Bouwdijk Bastiaanse	20
	Graham and Meigs16	25-30
	Only in Groups I and II	10
h .	den Hoed ¹⁷ in Groups I and II	10

There may be local postoperative recurrences when the operation has not been sufficiently extensive to remove all tissues containing cancer cells or when cancer cells have been implanted into the wound during operation.

So far it has not yet been possible to determine sensitivity to radium by cytological examination or biopsy. Perhaps someone will succeed in doing so in the future. In that event cases of radium-resistant carcinoma might be operated on. 18, 19, 20 Several investigators have shown that there are variations in resistance. Regaud²¹ believed that resistance to radium might also be caused by repeated irradiation. Therefore he recommended continuous administration of a large dose of radium over a short period. If this were true, it might explain the poor results obtained with irradiation in recurrences following radium therapy.

As radical hysterectomy was performed after the patient had been given a full dose of radium in a large number of cases treated in our clinic since October, 1950, we have been able to study the action of radium rays on carcinomatous tissue. The results are shown in Table VI.

TABLE VI. ACTION OF RADIUM RAYS ON CARCINOMATOUS TISSUE

Number of surgical specimens examined	196
No tumor cells found	115
More or less markedly degenerated cancer cells	73
Cancer cells showing no visible changes	8

Possibly the malignant cells observed may have disappeared later. No serial sections were made, so that the number of positive cervices may have been larger.

Several investigators have drawn attention to the fact that recurrences may occur even twenty-five years later, especially after radium therapy.

Morton²² even found this to be so in 29 per cent of the cases. In my opinion these recurrences probably are not true recurrences, but other carcinomas appearing in the same precarcinomatous tissue in which the initial carcinoma developed.

Postoperative local recurrences cannot occur unless the operation has been incomplete or living cancer cells have been implanted into the wound during operation

Metastases.—It has become increasingly doubtful whether x-rays have any noticeable effect on lymph node metastases in the true pelvis.²³ Carcinomatous lymph nodes can be removed for certain only by surgical methods. Too great expectations should not be entertained, however. Recovery persisted in only about 20 per cent of the patients in whom carcinomatous lymph nodes were removed. Not much has been published in the literature concerning involvement of the regional lymph nodes in patients who were not irradiated.

TABLE VII. POSITIVE LYMPH NODES

AUTHOR	YEAR	GROUP	PER CENT
Meigs ²⁴	1951	Group I	17.5
		Group II	32.1
Read ²⁵	1948	Group I	20-25
		Group II	30-35
		Group III	40-50
Taussig ²⁶	1943	Group II	26.8
		(preoperative x-ray i	rradiation)
Javert27		Group I	11.4)
		Group II	$\frac{11.8}{22.0} 17$
		Group III	33.0
		Group IV	80.0)
Navratil ²⁸ (results obtained by	8 authors)	Group I	11.24 ± 1.61
	1	Group II	23.10 ± 2.12
van Bouwdijk Bastiaanse ²⁹	1953	Group I	17.0
		Group II	33.0
		Group III	50.0

The percentage increase of surgical cases will be only about 4 per cent, viz., 20 per cent of 20 per cent. Meigs puts the permanent recovery rate in Group I at about 40 per cent when there are positive lymph nodes. Positive lymph nodes are found in only about 10 per cent of the cases, however. The five-year recovery rate in Group II is only about 10 per cent. A much larger number of positive lymph nodes is observed in this group, however (in about 30 per cent of the cases). Subsequent investigations will have to show whether the disadvantages of abdominal lymphadenectomy are counteracted by the gain.

Damage Resulting From Treatment

I shall merely give a summary of what I have stated on the subject in Meigs' book. Possible damage is caused by:

Radium: Ranging from proctitis or cystitis to rectovesicovaginal fistulas. The ovaries may be destroyed.

Wertheim's operation: Ureteral fistulas. Impairment of the innervation of the bladder.

Schauta's operation: Impairment of the innervation of the bladder.

Postoperative vesicovaginal or rectovaginal fistulas do not occur, unless there has been a lack of skill on the part of the surgeon.

Briefly, it may be said that every method has its advantages and disadvantages. Is it possible to reduce the risk of damage or prevent it?

Impairment of the innervation of the bladder: Several nerves enter the bladder at the level of the insertion of the ureters. Prolonged severe functional disturbance of the bladder no longer occurs in the Amsterdam Clinic, since more tissue has been left in place at the site where the ureters empty into the bladder.

Ureteral fistulas: These are due to injury caused during operation or to necrosis. In my opinion injury to the ureter may always be avoided, unless resection is done intentionally in view of the spread of the careinoma. I have twice injured the ureter, but never cut it through completely, when performing Schauta's operation. The injury occurred shortly after a variation in technique, i.e., at a time when I had not yet gained sufficient experience in the altered technique. Ureteral fistulas due to necrosis occur only after Wertheim's, never after Schauta's operation. In any case, I have never observed this. The necrosis may be caused by the deficient blood supply resulting from the ligation of too many blood vessels. The risk of necrosis is very liable to increase when the ureter has lost contact with the surrounding tissue over some distance. When Schauta's operation is performed, the ureter always remains in contact with the surrounding tissue.

Selection of the Method of Treatment

In my opinion the chance of recovery will be greatest if one therapy is employed in one case, and another in other cases. Therefore, individual factors should be given particular attention when a method is selected. A combination of various procedures might also improve the results. In recent years radium therapy has increasingly been combined with surgical treatment. may be expected to result from this method. Preoperative treatment with radium should reduce the risk of cancer cells being implanted. It might be that cancer cells are liable to be conveyed through the lymphatics or blood vessels as a result of the maneuvers performed during the operation. may be prevented by destruction of the cells by preoperative irradiation with radium. But even then I believe hysterectomy to be advisable to prevent the development of another carcinoma in the cervix. When active cancer cells persist after irradiation, the risk of metastasis resulting from surgical maneuvers will be smaller if part of the carcinoma has been destroyed. Another advantage would be that, if less tissue could be removed at operation than was anticipated, tissue which has received a full carcinoma dose would be left behind. When an abdominal operation is performed after preoperative treatment with radium, the regional lymph nodes may be removed as well.

Cancer in situ: No metastases can occur unless there has been an infiltrating growth. Accordingly lymph node dissection is unnecessary. As one can never be completely sure that no infiltrating growth has occurred in some place, I always perform an ordinary vaginal hysterectomy, during which only a cuff of the vagina is removed. Treatment is confined to amputation of the portio only in those cases in which preservation of the uterus is very important to the patient. Like Te Linde,³¹ we have frequently seen that the atypical epithelium had grown far upward into the cervical canal and also extended for some distance over the wall of the vagina. Therefore, amputation of the portio alone will always be attended with the risk of preinvasive cancer remaining.

Invasive cancer: Treatment with radium alone should be reserved for those carcinomas which are too widespread to be removed by operation only, and

S

e

8

e

S

r

e

e

e

d

e

those exceptional cases in which the general state of health is too poor to risk even a vaginal operation. Unlike Navratil, 10 I do not set an age limit. oldest patient was 82. In recent years we have treated all other cases with administration of a full dose of radium, combined with an operation. We have attempted treatment with radium prior to Wertheim's operation in 16 cases. Our experience has been similar to that of Meigs. Marked fibrosis of the tissue in which the lymph nodes are lodged, followed by catarrhal inflammation of the lymph nodes, is frequently seen to occur. Lymphadenectomy is difficult in these cases. Other authors experienced no difficulties. The dosage32 possibly plays a part in these cases. The difficulties involved in Schauta's operation are not, or are only slightly, increased by preoperative treatment with radium.

It is difficult to choose between Wertheim's and Schauta's operations. There is evidence from papers published to show that permanent recovery may occur in about 20 per cent of the cases showing positive lymph nodes. there has been no preoperative radium therapy, the risk of a contact metastasis and possibly of the transfer of cancer cells will have increased. In 50 Wertheim operations performed in our clinic one recurrence appeared in the apex of the vagina, which can be attributed only to an implantation metastasis.

Details of the Methods of Surgical Treatment.

The advantages and disadvantages of the two operations are shown in the following survey.

Wertheim's Operation .-

Advantages: Regional lymph nodes may be removed. Possible benefit 4

per cent of the surgical patients.

Disadvantages: Increased operative hazards. Risk of ureteral necrosis. Increased risk of implantation metastasis without preoperative radium therapy. Lymphadenectomy more difficult, so that operation is less radical, when preoperative radium therapy has been given. Occasional impairment of function of the bladder.

Schauta's Operation.—

Advantages: Smaller operative hazard. No necrosis of the ureters. Preoperative radium therapy hardly increases the difficulty of the operation.

Disadvantages: Regional lymph nodes cannot be removed. Occasional im-

pairment of function of the bladder.

Some authors believe that more parametrial tissue can be removed by a vaginal than by an abdominal operation. In our opinion the parametrium may

be removed as far as the pelvic wall in either case.

We occasionally performed Schauta's operation, followed by a transperitoneal lymphadenectomy four weeks later or vice versa. In doing so, we found that Schauta's operation is followed by the development of so much cicatricial tissue that an accurate lymphadenectomy is no longer possible. When the operation has been preceded by lymphadenectomy, the uterus will have become so immovable and the ureters so deeply embedded in scar tissue that the operation is seriously hampered. So far we have not performed a lymphadenectomy some time after irradiation with radium. This would probably be impeded by changes occurring in the tissues.

We do not understand why extraperitoneal lymphadenectomy should offer

any advantage over transperitoneal excision of the lymph nodes.

Until recently a barely movable uterus was occasionally regarded as a contraindication both to Wertheim's and to Schauta's operations. opinion Schauta's operation was contraindicated in the event of a too narrow vagina. The results obtained with radium therapy in a too narrow vagina were extremely poor, however. Of 26 patients, only 5 had survived without recurrences after five years. Therefore, in recent years Schauta's operation was also performed in patients with a barely movable uterus or with a narrow vagina, after a preoperative treatment with radium. Wertheim's operation was preferred in some cases.

A brief summary of the choice of treatment follows below:

Stages I and II: Treatment with a full dose of radium, followed four weeks lated by Schauta's or Wertheim's operation; if need be, by x-ray treatment. In patients under 35, the ovaries are not removed and no postoperative irradiation is given. When surgical treatment is definitely contraindicated, the patient is treated only with radium and x-rays.

Stage III: Radium and x-ray therapy. The patient is examined four weeks later to determine whether a radical operation can still be performed. Partial exenteration of the pelvic organs is done, if necessary.

Stage IV: Radium and x-ray therapy. Total or partial exenteration, if necessary.

Carcinoma of the Cervical Stump: Radium therapy, followed by Schauta's operation, is quite feasible.

Carcinoma of the Cervix and Pregnancy: Preoperative treatment with radium, followed by radical hysterectomy, during the first months of pregnancy. Treatment with radium in the later months. A cesarean section, followed by Wertheim's operation, is performed when the child is definitely viable.

Technique

I wish to add a few words on technique. As Schauta's operation still is hardly ever performed in the United States, I shall discuss this procedure in more detail. It has been completely described in Surgical Treatment of Cancer of the Cervix, by Meigs, pp. 248-266. Therefore, I shall only briefly refer to the most important features. The most serious risks with which the operation is attended are loss of blood and infection. Therefore, the operation should not be started unless at least 3 L. of blood are available. To prevent infection, 1 million units of penicillin and 1 Gm. of streptomycin are administered on the day before operation. Treatment with these doses is continued until one week after operation. Administration of antibiotics after the seventh day will depend on circumstances. During operation penicillin and 1 Gm. of streptomycin are applied to the wound cavities.

Technique of Schauta's Operation.—A difficult vaginal operation is practicable only when the legs have been markedly flexed at the hip. When the patient has not been treated preoperatively with radium, the tumor is coagulated with a view to destroying cancer tissue which might possibly become separated during operation. To avoid the risk of implantation metastases and to prevent infection when there has been no preoperative treatment with radium, a wide vaginal cuff which is accurately closed over a gauze impregnated with alcohol (Fig. 1) is prepared. The alcohol serves to destroy possible loose cancer cells. This is followed by a bilateral episiotomy. Navratil² and Mitra perform the episiotomy before the vaginal cuff has been made. We commenced with Schuchardt's incision in only 8 cases. A metastasis, from which the patient died, appeared in the incision in one case. Schauta³ and Ludwig Adler,³ as well as Amreich,¹¹ Navratil,² and Mitra perform only a unilateral episiotomy. Formerly we also used this method. The view obtained in bilateral episiotomy is much better, however.

The rectum is dissected out; as this is done, the rectum is pushed backward with the fingers of the left hand, while the vaginal cuff is pulled upward. Then the bladder is dissected out. Initially it should not be pushed back with a retractor as this will reduce the visibility of the cervicovesical space. When the cervicovesical space has been cleft and the bladder pushed upward,

a fascia, extending from the bladder and inserted into the cervix, is encountered (Fig. 2). Inexperienced surgeons sometimes believe this to be the boundary of the bladder. An attempt to dissect out will lead into the carcinoma in that case. The fascia must be cut. Then the bladder is pushed upward with a retractor and the ureters are dissected out. The ureter will be localized most readily when the dissecting out starts from the wall of the bladder.

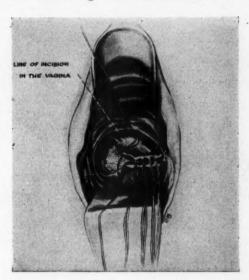


Fig. 1.—A vaginal cuff is closed over a gauze impregnated with alcohol. (From van Bouwdijk Bastiaanse in Meigs, J. V.: Surgical Treatment of Cancer of the Cervix, New York, 1954, Grune & Stratton.)

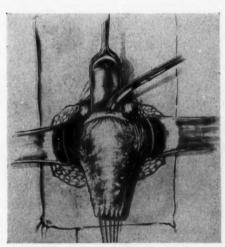


Fig. 2.—After the cervicovesical space has been opened, a fascia extending from the bladder and inserted into the cervix is encountered. This fascia must be cut.

When the tissue is dissected out as far as the walls of the bladder and the ureter, however, there is a considerable risk of severe impairment of function of the bladder. Therefore the ureter should be dissected out somewhat more backward (Fig. 3). When it has been exposed, the index finger of the left hand is placed in front of the ureter, pushed along the ureter, and inserted into the tissue, which surrounds the ureter like a tunnel (Fig. 4). Then this finger is pushed laterally until it is approximately against the wall of the pelvis. The ureter will remain on the dorsal side of the finger.

Next the cardinal ligament, starting from the levator muscle, is bluntly separated from the wall with a finger inserted between the cardinal ligament and pelvic wall (Fig. 5). Then the cardinal ligament is ligated directly against the pelvic wall and cut through (Fig. 6). Gradually more portions of the cardinal ligament are bluntly separated from the pelvic wall. The more resistant portions may contain blood vessels; therefore they have to be

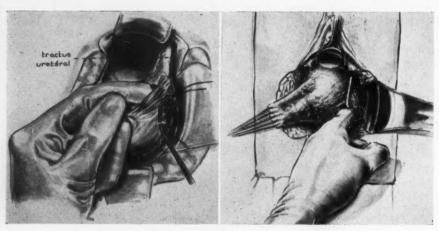


Fig. 3.

Fig. 4

Fig. 3.—The ureter is dissected. (From van Bouwdijk Bastiaanse in Meigs, J. V.: Surgical Treatment of Cancer of the Cervix, New York, 1954, Grune & Stratton.)

Fig. 4.—The index finger of the left hand is pushed into a tunnel through which the ureter runs.

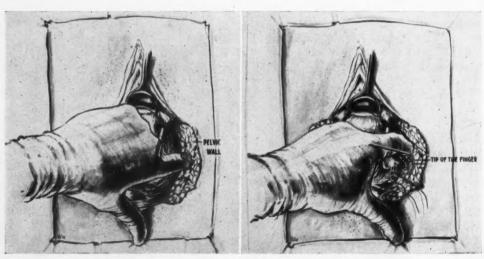


Fig 5

Fig. 6.

Fig. 5.—The cardinal ligament is bluntly separated from the pelvic wall. Fig. 6.—The cardinal ligament is ligated and cut against the pelvic wall.

ligated and cut through. Thus the entire parametrium will have been separated from the wall of the pelvis as far as the sacrum. Next the ureter is pushed far laterally. Where the ureter curves backward and upward, it crosses the uterine artery and vein. Medial to and as near as possible to the ureter this tissue is grasped with a clamp, ligated, and cut through (Fig. 7).

In that case the uterine artery and vein will almost always have been grasped. If they are not in the clamp, they will be very close to it. Then same tissue is grasped again. Previously we ligated the uterine artery and vein before cutting the cardinal ligament. We found that if the cardinal ligament is cut first, this will considerably increase the movability of the uterus, so that the latter can be pushed much further laterally and the uterine artery and vein, along with the portion of the parametrium situated at this site, can be cut much further out. The same is then done on the right side.

Next Douglas' pouch is opened. A large piece of gauze is inserted into the opening to hold back the intestines. A long retractor is used to push the rectum backward, while the uterus is pulled far forward with another long speculum. Thus the two sacrouterine ligaments and the other parametrial tissues are made tense (Fig. 8). The latter are ligated and cut as far laterally as possible. This is done about as far as the adnexa. Thereupon the plica vesicouterina is opened and the fundus of the uterus is displaced outward. The cervix, which increasingly protrudes during the cutting of the cardinal ligaments, returns into the vagina to some degree during the

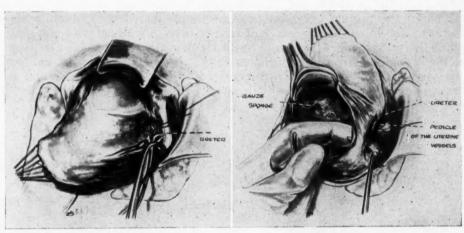


Fig. 7.

Fig. 8.

Fig. 7.—The uterine vessels with the surrounding tissue are clamped, ligated, and cut. (From van Bouwdijk Bastiaanse in Meigs, J. V.: Surgical Treatment of Cancer of the Cervix, New York, 1954, Grune & Stratton.)

Fig. 8.—The sacrouterine ligaments and parametrial tissue are made tense. (From van Bouwdijk Bastiaanse in Meigs, J. V.: Surgical Treatment of Cancer of the Cervix, New York, 1954, Grune & Stratton.)

outward displacement of the fundus. The pressure now occurring in the cuff might result in tissue slipping out between the gauze and the sutures and the implantation of cancer cells in the wound. Therefore the vaginal cuff is carefully wrapped in gauze. The pulling outward of the fundus uteri results in tension of the round ligaments and infundibulopelvic ligaments. The adnexa are grasped in an ovarian clamp. The round ligaments and infundibulopelvic ligaments are ligated and cut. The ovaries are usually left in place in women under 35. We have found that more parametrial tissue is removed when the adnexa are also excised. The peritoneal cavity is carefully closed. The pedicles are sutured extraperitoneally. The border of the peritoneum has been fixed with catgut threads during the cutting of the cardinal ligaments. The suture will be even more complete when the threads are tied together. As approximately one-third of the vagina is removed, an insufficient depth may result in difficulties during coitus. To retain a greater depth, the apex

of the vagina is sutured as far upward as possible to the stumps of the round ligaments. To facilitate the localization of the stumps, the ligatures applied to the round ligaments have not been cut.

Finally, the episiotomies are closed. The partially cut levator muscles are sutured with plain catgut, followed by the suture of the rest of the cut tissue, the wall of the vagina, and the skin. As the secretions discharged will dissolve catgut more rapidly, silk threads are used to suture the skin. Owing to the antibiotics which have been applied, the episiotomies nearly always heal by first intention. Usually the vagina is not plugged with a tampon. This is done only in the event of persistent loss of blood. A tamponade might result in laceration of the peritoneum, increasing the danger of peritonitis. The silk sutures are removed on the tenth day. An indwelling catheter is applied for at least twelve days.

Technique of Wertheim's Operation.—This is described only to the extent in which it differs from that of Meigs' operation. One of the disadvantages of Wertheim's operation, performed without preoperative radium therapy, is the danger of cancer cells being implanted into the wound. To prevent this, electrocoagulation is done and an extensive vaginal cuff is prepared as the first stage of the vaginal operation, a gauze impregnated with absolute alcohol is inserted, over which the vaginal cuff is very carefully closed with silk sutures. A gynecological tampon with penicillin in its depth is inserted into the vagina. Then the operation is continued abdominally. No clamps are used in ligating the tissues. When the cardinal ligaments as well as the pararectal and paravaginal tissues are ligated by aneurysm needles, a larger amount of tissue may be removed. A rigid clamp cannot completely follow the curves in the pelvis.

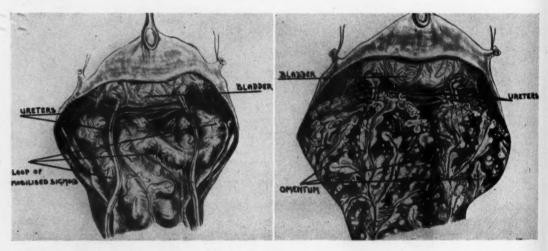


Fig. 9.

Fig. 10.

Fig. 9.—Dead spaces through which the isolated ureters run.

Fig. 10.—The dead spaces around the ureters are filled with a loop of the sigmoid and a pedicle flap of omentum is brought over the ureters, as to prevent development of a necrotic fistula.

One of the chief drawbacks to Wertheim's operation is the not infrequent appearance of necrosis of the ureter. Accordingly an attempt should be made to keep the blood supply at its initial level both during and after the operation. There always will be a certain reduction, as several blood vessels are ligated and cut. As a fall in blood pressure will result in a further decrease of the

blood supply, attempts should be made to prevent this. Therefore we do not regard a hypotensive anesthesia as advisable. On the contrary, we aim at maintaining the blood pressure level by administration of blood.

In the hope of increasing the blood supply during the postoperative period the left dead space around the ureter is filled with a loop of the sigmoid, (Fig. 9) which is mobilized if necessary, while a pedicled flap of omentum is brought over the ureters, or is inserted into the right dead space (Fig. 10). The extremity of the pedicle flap is sutured to the wall of the bladder at the site where the ureter empties into the bladder. Then the omentum will completely cover the isolated ureter. The flap of omentum is sutured far laterally to the peritoneum of the anterior abdominal wall to prevent ileus. After operation an indwelling catheter is applied for a minimum period of three weeks. Both after Schauta's and after Wertheim's operations the patient. is often unable to empty the bladder for a few weeks, or can do so only insufficiently. When there is retention in the bladder, there also will be retention in the ureters. The resulting tension of the wall causes constriction of the blood vessels. We observed no necrosis of the ureter in 35 operations performed in this way. We carried out experiments in dogs and rabbits to study whether blood vessels from a flap of omentum would continue to grow in a markedly isolated ureter. Fig. 11 shows the microscopic findings. The wide lumina beside and in the wall of the ureter probably are portions of the same blood vessel.

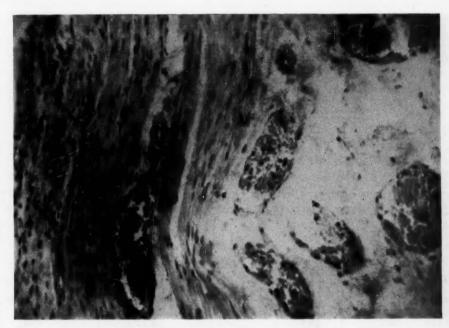


Fig. 11.—Photomicrograph showing wall of ureter on the left and adherent omentum. One blood vessel of the omentum has penetrated the wall of the ureter.

Results

The results obtained show that, as has also been reported elsewhere, the war has had an adverse effect. From 39.6 per cent during the period 1939-1946, inclusive, the five-year cure rate rose to 50 per cent in 1947 and 51.7 per cent in 1948. The five-year cure rate in the group of surgically treated patients was 50.2 per cent during the period 1939-1946, inclusive, 68 per cent

TABLE VIII. RESULTS OF TREATMENT, 1939-1946, INCLUSIVE

	NO. PATIENTS	NO. OF OPERATIONS (SCHAUTA)		ALIVE WITH NO EVIDENCE OF THE DISEASE AFTER 5 YEARS		OF PATIENTS OPERATED UPON	
	TREATED	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Stage I	121	96	79.3	67	55.4	53	55.2
Stage II	188	139	73.9	78	41.5	65	47.5
Stage III	104	0		21	20.2		
Stage IV	6	0		0			
Total	419	235	56.1	166	39.6	118	50,2

TABLE IX. RESULTS OF TREATMENT, 1947 AND 1948

	NO. PATIENTS TREATED	NO. OF OPERATIONS (SCHAUTA)		ALIVE WITH NO EVIDENCE OF THE DISEASE AFTER 5 YEARS		OF PATIENTS OPERATED UPON	
		NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Stage I	43	36	83.7	30	69.8	27	75
Stage II	33	23	69.7	19	57.6	15	65.2
Stage III	38	1		9	23.7	0	
Stage IV	4	0		2		0	
Total	118	60	50.9	60	50.9	42	70

TABLE X. RESULTS OF TREATMENT, 1949-1952, INCLUSIVE

	NO. PATIENTS TREATED (STAGE 0 NOT IN-	NUMBER OPERATIO		SCHAUTA + OR -	EVIDENCE	ALIVE WITH NO EVIDENCE OF DISEASE 1/7/1954		NO. PATIENTS OPERATED UPON		SCHAUTA + OR - RADIUM	
	CLUDED)	NO.	1 %	RADIUM	NO.	1 %	NO.	%	NO.	1 %	
1949.—											
Stage I	19	18	94.7	15	17	89.5	16	88.9	13	86.7	
Stage II	15	10	66.7	9	10	66.7	7	70	6	66.7	
Stage III	16	0			4	25					
Stage IV	3	1		1							
Total	53	29	54.7	25	31	58.5	23	79.3	19	76	
1950.—		-									
Stage I	18	15	83.3	15	13	72.2	11	73.3	11	73.3	
Stage II	20	11	55	11	12	60	8	72.2	8	72.2	
Stage III	21	4	14.3	3	5	23.8	2	50	2	66.7	
Stage IV	3	1		1	1		1		1		
Total	62	31	50	30	31	50	. 22	71	22	73.3	
1951.—											
Stage I	30	28	93.3	28	24	80	23	82.1	23	82.1	
Stage II	22	16	72.7	15	12	54.6	9	56.3	9	60	
Stage III	16	3	18.8	3	7	43.1	1		1	33.3	
Stage IV	3	0			0						
Total	. 71	47	66.2	46	43	60.6	33	70.2	33	71.7	
1952.—											
Stage I	40	39	97.5	29	35	87.5	34	85	26	89.7	
Stage II	30	28	93.3	26	21 .	70	20	71.4	19	73.1	
Stage III	15	4	26.7	4	7	46.7	4	100	4	100	
Stage IV	5	0			2	40					
Total	90	71	63.9	59	65	72.2	58	81.7	49	83.1	

in 1947, and 71.4 per cent in 1948. The cure rate for radium therapy was 26.1 per cent during the period 1939-1946, inclusive, and also 26.1 per cent in 1947 and 1948. The results obtained in the following years will probably not be less, rather higher than in 1947 and 1948. The period which has elapsed is still too short to form an opinion on the effect of the highly individual therapy introduced by me since October, 1950. I feel justified, however, in continuing with this highly individual method of treatment, which is characterized by the fact that each method of treatment has its own indications. Thus effective treatment of carcinoma requires a team, which includes both a good radiologist and a skilled surgeon in addition to nontechnical physicians.

Summary

The treatment of carcinoma of the cervix uteri in the Gynecological Clinic of the University of Amsterdam is discussed. In forming an opinion on the selection of methods of treatment, attention is drawn to the fact that, owing to recent improvements in the field of blood transfusion and antibiotics, primary mortality has declined to below 1 per cent, operations can also be performed on patients previously regarded as poor operative risks, and a much more radical operation can be performed. Cure rates, calculated only with regard to the number of surgically treated patients, have a merely relative value. For this rate will also depend upon the proportion of hospitalized patients operated upon. Therefore a complete survey of all patients with carcinoma of the cervix is essential to determine the most effective method of treatment.

Positive lymph nodes are found in 10 to 12 per cent of the patients of Group I and 30 to 40 per cent of those of Group II. According to Meigs, a 5 year cure occurs in 40 per cent of the cases in Group I and in 9 to 10 per cent of the cases in Group II, when positive lymph nodes have been found. Accordingly lymphadenectomy may result in an increase of the recovery rate of the patients operated upon by 4 per cent. Drawbacks to lymphadenectomy are that it becomes much more difficult, and therefore is less radical, after radium therapy. In addition, the number of ureteral fistulas increases.

The advantages and disadvantages of the various methods of treatment are discussed. From these data it is concluded that all methods, alone or combined, have their individual indications.

To reduce the risk of the occurrence of ureteral fistula in an abdominal operation, the dead spaces about the ureters are filled with a mobilized loop of sigmoid or with a pedicled flap of omentum. Microscopic examination showed that tissue grows from the omentum into the isolated ureter of dogs or rabbits.

The following scheme of treatment is observed in the Gynecological Clinic of the University of Amsterdam:

Stages I and II.—Treatment with a full dose of radium, followed four weeks later by Schauta's or Wertheim's operation. If need be, x-ray treatment. The ovaries are not removed and no postoperative irradiation is given in patients under 35. When surgical treatment is definitely contraindicated, the patient is treated only with radium and x-ray.

Stage III.—Radium and x-ray therapy. The patient is examined four weeks later to determine whether a radical operation can still be performed. Partial exenteration of the pelvic organs, if necessary.

Stage IV.—Radium and x-ray treatment. Total or partial exenteration if necessary.

Radium therapy, followed by Schauta's operation, is quite feasible in operable cases.

Carcinoma of the Cervix and Pregnancy .-

Stages I and II: Preoperative treatment with radium, followed by radical hysterectomy, during the first month of pregnancy. Treatment with radium in the later months. A cesarean section, followed by Wertheim's operation, is performed when the child is definitely viable.

Stages III and IV: Radium therapy and subsequent cesarean section, followed by a radical abdominal operation if possible.

The technique of Schauta's operation is described in detail. The results obtained are reported. The five-year cure rate was much lower during the war years than during the subsequent period, especially in the surgically treated cases (50.2 per cent as against about 70 per cent). It is concluded that the highly individual method of treatment introduced since October, 1950, will probably yield the best results.

References

- 1. Wertheim, E.: Die erweiterte abdominale Operation bei Carcinoma Colli Uteri, Berlin and Wien, 1911, Urban and Schwarzenberg.

- 2. Bonney, Victor A.: A Textbook of Gynaecological Surgery, ed. 6, New York, 1952, Paul B. Hoeber, Inc.
 3. Pratt, J. H.: S. Clin. North America 31: 1063, 1951.
 4. Meigs, Joe V., editor: Surgical Treatment of Cancer of the Cervix, New York, 1954, Grune & Stratton.
- Grune & Stratton.

 5. von Peham, H., and Amreich, I.: Operative Gynecology, Philadelphia, 1934, J. B. Lippincott Company.

 6. Stoeckel, W.: Zentralbl. Geburtsh. u. Gynäk. 55: 53, 1931.

 7. Mitra, Subodh: In Meigs, J. V., pp. 267-280, Grune & Stratton, 1954.

 8. Corscaden, J. A.: Gynecologic Cancer, New York, 1951, Thos. Nelson and Sons.

 9. de Bruïne, T. L. A.: De behandeling van het carcinoma colli uteri, Amsterdam, 1954, Scheltema & Holkema, p. 62.

 10. Navratil, Ernst: In Meigs, J. V., pr. 218-247.

 11. Amreich, J.: Klinische Fortschritte in der Gynäkologie, Tassilo Antoine. 1954, Munich, Urban & Schwarzenberg.

- Urban & Schwarzenberg.
- 12. German Gynecological Congress: Arch. Gynäk., vol. 173, 1942.
- 13. Heyman, J., Kottmeyer, H. L., and Segerdahl, C. O.: Acta obst. et gynec. scandinav. 32: 65, 1932.

- 14. Results, Department of Obstetrics and Gynecology, University of Amsterdam.
 15. Eymer, H.: In Leitz and Amreich, editors: Biologie und Pathologie des Weibes, Berlin, 1953, Urban & Schwarzenberg, Band V, Teil 2, p. 317.
 16. de Bruïne, T. L. A.: De behandeling van het carcinoma colli uteri, Amsterdam, 1954, Scheltema & Holkema, p. 104.

- Scheltema & Holkema, p. 104.

 17. den Hoed, D.: Nederl. tijdschr. v. verlosk. en gynaec. 45: 71, 1942.

 18. Graham, Ruth: Surg., Gynec. & Obst. 84: 153, 1947.
 Graham, Ruth, and Meigs, Joe V.: Am. J. Obst. & Gynec. 58: 843, 1949.
 Graham, Ruth, and Meigs, Joe V.: Surg., Gynec. & Obst. 93: 767, 1951.

 19. Glücksmann, A., and Spear, F. G.: Brit. J. Radiol. 18: 313, 1945.
 Glücksmann, A. and Way, S.: J. Obst. & Gynaec. Brit. Emp. 55: 573, 1948.
 Glücksmann, A.: Twelfth British Congress of Obst. & Gynaec. 1949 (Introd. papers).

 20. Bouwer, W. F., and Ghilain, A.: Nederl. tijdschr. v. verlosk. en gynaec. 52: 193, 1952.

 21. van der Heyden, C. A. M.: Enige beschouwingen aangaande het carcinoma colli uteri,
 's Gravenhage, 1948, N. V. Uitgevery W. P. van Stockum & Zoon.

- Morton, D. G.: Am. J. Obst. & Gynec. 57: 685, 1947.
 Javert, C. F.: In Meigs, J V., p. 285.
 Meigs, J. V.: Am. J. Obst. & Gynec. 62: 854, 1951.
 Read, C. D.: Am. J. Obst. & Gynec. 56: 1021, 1948.

- Read, C. D.: Am. J. Obst. & Gynec. 56: 1021, 1948.
 Taussig, F. J.: Am. J. Obst. & Gynec. 45: 733, 1943.
 Javert, C. F.: In Meigs, J. V., p. 85.
 Navratil, Ernst: In Meigs, J. V., p. 219.
 van Bouwdijk Bastiaanse, M. A.: Kankerjaarboek, Amsterdam, 1953, J. H. de Bussy.
 McCrea, L. E.: In Meigs, J. V., p. 126.
 Te Linde, R. W.: In Meigs, J. V., pp. 130-139.
 Currie, D. W.: Proc. Roy Soc. Med. 45: 327, 1952.
 Schauta, F.: Die erweiterte vaginale Totalexstirpation des Uterus bei Collumcarcinom, Wien-Leipzig, 1908, Safar.
 Adler, L.: Am. J. Obst. & Gynec. 23: 332, 1932.

Discussion

DR. HERBERT E. SCHMITZ.-Professor Bastiaanse, we in Chicago are jealous of our tradition. We recognize your interest in attaching the name of Wertheim to the procedure of radical hysterectomy and lymph node dissection. At the same time we find in the literature that our own Emil Ries described in 1895 the following operation, and I quote,

The cancerous tissue is cut and scraped away, the bleeding surface is thoroughly cauterized and shut off by flaps of the vaginal wall which are sewed together over the os. The patient is then put in the Trendelenburg position; removal of the ovaries, tubes, uterus and broad ligaments is carried out. Then taking the bifurcation of the common iliac artery as the starting point, the peritoneum is cut open on the posterior wall of the pelvis, and the glands are dug out with the surrounding connective tissue by the sole aid of the fingers. The peritoneum is closed with sutures.

Clark, in 1895, introduced the ureteral bougies and advocated the excision of a much larger portion of the vagina than usual.

Wertheim, in 1907, gave exactly the same description of the operation which he called

The Professor has demonstrated quite clearly the safety of the surgical procedure of the Schauta and the Wertheim operations as he describes them, although there have been improvements due to improved surgical technique, in the choice of anesthesia and anesthesiologists, in the use of the antibiotics, in the combating of shock, and the use of blood in great quantities. These, too, have been responsible for the improved results with irradiation therapy. McKelvey has shown that it is extremely important to combat infections and to improve nutrition if you expect to obtain maximum results with irradiation therapy.

It is of interest that, in the 196 cases where the Schauta operation was performed following an "adequate dose" of irradiation, although that dose has not been defined, 115 of those patients had no residual cancer. Seventy-three additional cases showed markedly degenerated cells four weeks following the application of irradiation. We must realize that the irradiation effect had not been entirely expended at the end of a month, or probably not at the end of six or eight weeks. Tumor cells can be viable as long as six months. Therefore, we can only accept the fact that there were 8 patients who still had viable cancer cells and who could not have survived without the surgical procedure, and that there were 188 patients in whom there was no viable tumor and in whom the surgical procedure might have been avoided. The question we must always ask ourselves, if we curtail the extent of the dissection as Bastiaanse has advocated in order to prevent the complications with the bladder and ureters, is, are we then defeating the purpose for which the operation was originally intended? We have been told by the proponents of radical surgery that in the first place there are fewer complications, in the second place, the structures are removed so there can be no future disease within those structures, and in the third place, that carcinoma in the lymph nodes becomes resistant to irradiation and, therefore, dissection of the nodes is imperative.

Bastiaanse demonstrates that only 4 per cent improvement in results can be gained by this means and, therefore, he discounts the Wertheim procedure and is satisfied with the removal of the uterus and the parametrial tissue. I am not ready to accept the statement that the invaded nodes are resistant to irradiation. I believe this has been demonstrated quite conclusively to be in error because the percentage of positive nodes in irradiated patients is fewer than in nonirradiated patients, and Meigs, who was one of the strongest advocates of that dictum, is now admitting that not all disease in nodes is radioresistant. Graham recently has stated that he finds that certain patients are better treated with irradiation, and these are the cases with the highest percentage of nodal invasion. Based on this Meigs says, "I have for years been in error. I must admit that the nodes are not always resistant to irradiation."

It is extremely interesting to hear the description of Döderlein and Wertheim's exchange of words at the German Congress, and his opinion that at that time surgery had reached a plateau and there could be no further improvement. This has been said so often by the surgeons, namely, that irradiation has reached a plateau and that no further changes or improvements can be expected by this means. Everett recently published the results of his study at Johns Hopkins on urinary tract injuries following both operative procedures and irradiation, and I believe has come to the conclusion that about 30 per cent of the irradiation survivals will show some permanent change which is the result of injury by the rays, but the damage resulting in fistulas is not necessarily in the early cases, therefore excusable and not always due to lack of skill. It does take skill to perform the radical operation just as it takes skill to administer and apply irradiation.

I have the results in a comparable group of cases, treated in our clinic between 1933 and 1948. There were 51 recurrent and 271 primary cases, or a total of 322 proved carcinomas of the cervix.

If we break these down into the Schmitz classification, Group I and Group II represent Stage I of the International classification. You will notice that in the over-all five-year survivals in the primary cases we include all of the cases in the four groups. Those patients who had previous surgery or irradiation before coming to us are excluded from this study because I do not believe they should be included in a comparison of this type. We have 87.5 per cent of the Group I cases surviving five years later. Of the 3 patients lost from follow-up, the first died three years after therapy of a pulmonary embolus following a cholecystectomy. Autopsy revealed no evidence of disease. The second patient had been lost after four years but had no evidence of disease up to that time. The third patient succumbed to coronary heart disease. Autopsy revealed no evidence of disease.

In Group II, 65.1 per cent were free of disease for an over-all survival rate of 43.1 per cent in the four groups.

The 40.5 per cent survival in Group III and 11.4 per cent in Group IV cases clearly indicate that in some instances disease in regional nodes can be destroyed by irradiation, otherwise none of these patients could survive five years and over.

Frequently we hear discussion relative to the resistance and the sensitivity of tumors. In all of these cases all tumors were graded according to Broder's classification into Grades I, II, III, IV, and adenocarcinoma. There has been no evidence in our study and in other published work that you can foretell by microscopic appearance that you are dealing with a sensitive or resistant tumor. We have resorted to a trial of irradiation therapy and feel that this is extremly important. It is our procedure to use primary irradiation and reserve surgical procedures for those patients who clinically demonstrate that they have radio-resistant disease. Weekly cytologic studies and repeat biopsy are used to study the response of the tumor. If after completion of therapy the tumor cells show any little effect these patients are segregated for more careful study, so that surgical therapy can be instituted

n

d

e-

1-

d

st

t.

h

n

ot

98

d

n

S

s

S

e

3

t

S

y

n

a

n

t

1

h

1

e

e

the instant that the diagnosis of resistant tumor is established. We in our laboratory are trying to repeat the work of the Grahams and Meigs in determining the SR factor; however, to date our efforts have failed because of our inexperience.

In 1933, we first had available the so-called supervoltage or high voltage x-ray therapy. That is why this group of patients is taken from that period of time.

In the recurrent cases, those partly or unsuccessfully treated before coming to our clinic, there were 88.8 per cent of the Group II patients treated with irradiation who survived; 38.4 per cent in Group III, and 7 per cent in Group IV, which is a 29.4 per cent survival rate in the recurrent disease. I think we will all admit that in cases where primary treatment has failed and where there is recurrence or persistence of disease there is a change in the response of the tumor to all types of therapy. I believe this is in line with our present-day thinking relative to the treatment of carcinoma of the cervix.

We feel that primary irradiation gives us the best end results and that we have no evidence that we could improve our results by subsequent surgical procedures in the earlier stages of the disease. If the patient following irradiation continues to have Grade III smears showing abnormal cells persisting after three or four months, though there is apparent clinical healing, we still biopsy the cervix and continue to do so until there is no further positive activity or persistence of the disease. Sometimes a period of six months will elapse before the smears are completely negative. If at the end of six, seven, or eight months the smears are still positive, and if the amount of irradiation has been adequate, there will be fibrosis or fibrosclerosis but not enough to impede surgery, so we recommend dissection of the pelvic nodes and a radical hysterectomy. If the patient does not show adequate clinical healing or if the disease seems to remain active and the biopsy and smear show very little irradiation effect, then, of course, we are dealing with a resistant type of tumor, and as soon as the trial of irradiation is finished, we prepare the patient for a surgical procedure.

We do not have sufficient cases since the beginning of the present study to evaluate irradiation to show five-year results which would be convincing.

In the study of the end results obtained by surgical procedures we must keep constantly in mind the fact that the complications to the urinary tract are equal in severity and occurrence to those experienced in a properly irradiated series.

DR. A. F. LASH.—I should like you to keep in mind that Dr. Bastiaanse's results are those of many years of concentrated work on carcinoma of the cervix through the vaginal route. Then we come to the extensive experience of Dr. Schmitz with radium, and we can well appreciate that we are dealing with two experts in their own fields. Today, similar good results have been obtained by the abdominal route.

Extensive experience in cancer work comes only in centers of concentrated material. Since it is possible for a man to become expert in only one field in a lifetime, it becomes more and more evident that only in cancer therapy centers can one obtain the near ideal combination of therapy. Thus each patient can be properly evaluated by a team of medical men, gynecologist, radiotherapist, and pathologist. Thereby the acme of therapy can be achieved with improving results.

The variable factors, the biologic reaction of the patient and the pathologic character of the invading neoplasm, are recognized and their variation in response to irradiation is also well known. Therefore, it becomes quite important to the patient to be treated not by only a radiotherapist or surgeon but rather by that combination of experts who will direct the form of therapy required by the individual patient and not only one form of therapy for all patients.

Therapy is not only more effective in early lesions but also it is most advantageous to determine as soon as possible when a lesion is radioresistant or when there is a recurrence, when further irradiation is not only of no avail but may even be harmful.

Since we are still seeing far-advanced and neglected or mistreated instances of cancer when the possibility of cure has passed, some palliation may be rendered. The hopelessness and futility of therapy in these instances may be decreased.

Only by concentrating the patients in centers manned by staffs of experts can further progress be made in our knowledge of cancer and improvement in our therapeutic results.

PROFESSOR BASTIAANSE (Closing).—I did not hear Dr. Schmitz mention any of the late recurrences. There are publications which mentioned that after radium treatment recurrences may occur late, even after many years. I believe the reason for these late recurrences is that precancerous tissue, upon which the carcinoma had developed, is not destroyed. After a radical hysterectomy the local cancer is removed, so that a local recurrence cannot occur. If by operation we still should have a high primary mortality then, of course, there would still be much more to be said for radium treatment alone. Now that the primary mortality has fallen so low that it is negligible, I believe this is a reason for more extensive operations being performed in these cases.

As for radium resistance, we only had 8 cases in which nothing could be seen after radium irradiation. In the group with "more or less markedly degenerated cancer cells" are cases with severe, but also cases with only slight, regression of the cells. Up until now we cannot say whether living cancer cells would not have disappeared later, but it may also be possible that cancer cells with slight regression can cause a local recurrence.

In my opinion irradiation of radium before operation may be advantageous. I believe that perhaps very close to the source of the radium all cancer cells are destroyed, but that this will not always happen at some distance. These cancer cells might be spread during operation, due to the operative maneuvers. But the smaller the number of cancer cells, the smaller will be the chance for spread.

I agree with Dr. Schmitz' statement that Meigs now agrees that cancer cells in the lymph nodes can be destroyed by irradiation.

Since October, 1950, we have been using highly individualized treatment for cancer patients in our clinic. We are still in an experimental stage; we study the patients to determine which should be treated by irradiation, which by operation, and which by both. We know that the slow-growing cancers metastasize much later than the fast-growing ones, and therefore perhaps the patients who have a long period between the onset of symptoms and admission to the hospital should be treated by the Schauta operation and the others by the Wertheim.

CARCINOMA OF THE CERVIX WITH EARLY STROMAL INVASION*

CHARLES B. WHEELER, JR., M.D., KANSAS CITY, Mo.

(From the Department of Pathology and Research, St. Luke's Hospital)

THE past decade has seen a remarkable increase in the daily contacts between gynecologists and pathologists. Under the influence of such men as Papanicolaou and Ayre, there has developed a certain symbiosis between the two specialties, which also benefits the patient.

A tabulation of our material at St. Luke's Hospital shows that 1,183 gynecological surgical specimens were received in 1950 for histologic examination. That same year there were 167 cervical smears submitted for Papanicolaou stains. By 1954 the number of gynecological specimens had increased to 2,795 and there were 1,272 Papanicolaou smears examined. This represented a 150 per cent increase in the surgical material and an increase of over 750 per cent in smears over the five-year period.

Material

In all, some 9,715 gynecological specimens and 3,794 smears were examined from 1950 through 1954. This material was screened for cervical lesions which would fall into the following arbitrary categories:

A. Precancerous Metaplasia.—This descriptive term was recommended by Carson and Gall,¹ and seems preferable to basal-cell atypia, nearo-cancer, and in situ atypia. The condition is characterized by a piling up of atypical basal cells beneath a narrow surface layer of adult squamous cells which maintain the normal horizontal flattening in relation to the basement membrane (Fig. 1). It is thought to be reversible and is sometimes associated with cervicitis. Positive Papanicolaou smears may result from the sloughing of the atypical basal cells.² Precancerous metaplasia should be differentiated from benign metaplasia, where the glandular epithelium of the endocervix changes into a stratified squamous epithelium showing a normal morphology and stratification.

B. In Situ Carcinoma.—The atypia, hyperchromatism, and dyskeratotic arrangement, which were confined to the basal layers in precancerous metaplasia, have increased to involve the entire thickness of the epithelium. The cells are usually arranged perpendicularly to the basement membrane (Fig. 2). Whether this lesion is reversible in any given case is difficult to say, but such reversion has been observed following pregnancies, during which positive biopsies of in situ carcinoma were obtained and left untreated.³

C. In Situ Carcinoma With Gland Penetration.—In this group, the through and through, dyskeratotic, atypical changes of in situ carcinoma involve not only the surface epithelium, but are seen extending down into the endocervical glands (Fig. 3). This extension is sometimes referred to as gland invasion, but gland involvement or gland penetration are preferable terms since it still represents an intraepithelial growth which has not shown any invasive tendency.

^{*}Aided by a grant from The John W. and Effle E. Speas Memorial Trust Fund.

Fig. 1.

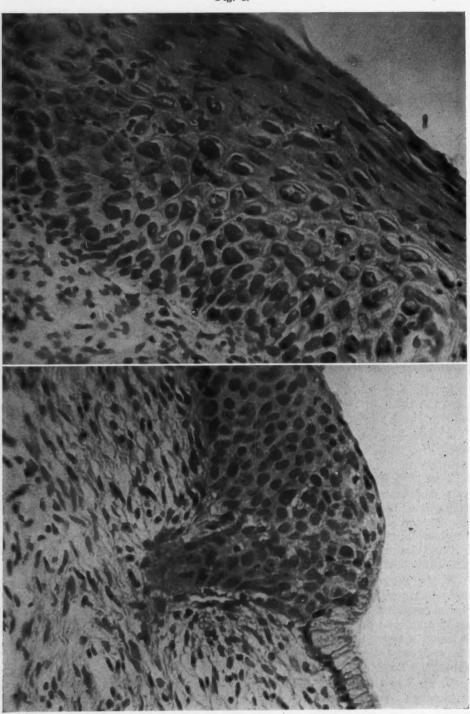


Fig. 2.

Fig. 1.—H.P. Photomicrograph showing precancerous metaplasia. Note that the upper third of the squamous epithelium shows normal stratification and the basal layers are hyperchromatic and irregularly stratified. (×400; reduced ½.)

Fig. 2.—H.P. Photomicrograph showing carcinoma in situ. Note that the squamous side of the squamocolumnar junction shows complete dyskeratosis, mitoses, and nuclear variants. (×400; reduced ½.)

D. Early Stromal Invasion.—A recent article by Fennell⁴ provides excellent photomicrographs of this lesion. It is characterized by a few malignant cells wandering out from the confines of an epithelium involved by in situ careinoma, either on the surface or from within an endocervical gland (Fig. 3). It is sometimes extremely difficult to decide whether a particular case represents marked gland penetration or early stromal invasion. The line which separates these two conditions is quite vague and often a single group of cells in as many as 40 sections will determine the final diagnosis in a given case. It is this group of cases that this article intends to emphasize.

E. Unqualified Invasive Carcinoma of the Cervix.—The line separating this category from the previous one must, of necessity, be a subjective one for the pathologist to determine. All lesions showing more than very superficial invasion must be considered as unqualified invasive carcinoma. The justification for a clinical separation of these two degrees of invasion will be discussed later.



Fig. 3.—L.P. Photomicrograph showing in situ carcinoma with gland penetration on the right and early stromal invasion on the left. Note that the nest of cells in the lower left is sending out thin cords of atypicalcells into the surrounding stroma. (×85; reduced 1/6.)

Incidence

Table I shows the frequency with which these five lesions occurred in our material from 1950 through 1954. The number of Papanicolaou stains is included in the seventh column because the steady increase in the number of cervical lesions discovered each year is the result of the increasing numbers of smears examined. Another feature of interest was the relative scarcity of in situ lesions without gland penetration; instances of in situ carcinoma with gland penetration were two and one-half times as frequent.

TABLE I. FREQUENCY OF EPITHELIAL NEOPLASIA OF VARIOUS TYPES FROM 1950 to 1954

YEAR	PRE- CANCEROUS META- PLASIA	IN SITU	IN SITU CARCINOMA WITH GLAND PENE- TRATION	EARLY INVASIVE CARCINOMA	DEEPLY INVASIVE CACINOMA	PAPANIC- OLAOU SMEARS	TOTAL CERVICAL LESIONS
1950	5	1	1	4	10	167	21
1951	8	1	2	2	7	472	20
1952	7	5	1	3	15	731	31
1953	5	1	9	5	19	1,152	39
1954	9	2	10	9	14	1,272	44
Total	34	10	23	23	65	3,794	155

Pathogenesis

We feel that these five categories represent consecutive changes which the cervical epithelium undergoes in the transition from normal stratified squamous epithelium to unqualified invasive carcinoma. The arguments in favor of this proposition are quite convincing and have gained general acceptance.

Hertig and Younge⁵ found that in situ carcinoma and invasive squamouscell carcinoma of the cervix occurred with about the same frequency. This equality of occurrence should hold only when the material examined represents a cross section of the general female population. We do not feel that our material, with 88 cases of invasive carcinoma and 33 cases of in situ carcinoma, is evidence against this equal incidence, because our figures represent women often coming to the doctor's office because of some pelvic disturbance.

Hertig and Younge also found that the average patient with invasive carcinoma was several years older than the one with an in situ lesion. This age difference is strong evidence that invasive carcinoma of the cervix, like squamouscell carcinoma elsewhere in the body, may take several years to develop.

Average Ages of Patients with in Situ Carcinoma, Early Stromal Invasion, and Unqualified Invasive Carcinoma

It was in an effort to discover whether these cases of very early invasion were more akin to in situ carcinomas, from whence they arose, or the unqualified invasive carcinomas to which they progressed, that we divided our 88 cases of invasive carcinoma into two groups. By arbitrarily screening these cases, we were able to find 23 in which the slides showed such minimal invasion that the Chairman of the Department of Pathology, Dr. Ferdinand C. Helwig, thought it worthy of mention as a very early lesion.

Our 33 patients with in situ carcinoma had an average age of 40.5 years; the 23 with early stromal invasion, an average age of 44.0 years; and the 65 with unqualified invasive squamous-cell carcinoma of the cervix, an average age of 52.8 years.

TABLE II. AVERAGE AGE AND INCIDENCE OF EPITHELIAL NEOPLASIA

		S HOSPITAL, CITY, MO.	FREE HOSPITAL FOR WOMEN BROOKLINE, MASS.		
	NO. OF CASES	AVERAGE AGE	NO. OF CASES	AVERAGE AGE	
In situ carcinoma	33	40.5 years	201	38.0 years	
Early stromal invasion	23	44.0 years	38	42.2 years	
Deeply invasive carcinoma	65	52.8 years	1,314	50.8 years	

Wheeler and Hertig⁶ recently made a similar analysis of cases at the Free Hospital for Women. They reported 201 cases of in situ carcinoma at an average age of 38.0 years; 38 cases of early stromal invasion at an average age of 42.2

years; and 1,314 cases of invasive squamous cell carcinoma of the cervix, subdivided by clinical staging, at an average age of 50.8 years. A comparison of these two series is shown in Table II. They provide a chronological justification for this borderland of "early stromal invasion" which separates in situ carcinoma from invasive carcinoma of the cervix. It is a lesion which causes difficulty for the pathologist in diagnosis and for the gynecologist in treatment, yet seems to be occurring with increasing frequency as more and more early lesions are seen by the examining physicians.

Treatment of Early Stromal Invasion

The pathologist sees invasive carcinoma ranging from a few cells wandering out from the confines of a gland to a complete obliteration of the normal architecture by anaplastic tumor cells. The knowledge that many physicians treat these two distinct and separate conditions in the same way, causes considerable anxiety. A pathologist needs to perform an autopsy on only one 30-year-old woman who has died from the effects of well-administered irradiation, in order to become painfully aware of the responsibilities which accompany the description of a few malignant cells in the superficial cervical stroma. He feels obligated to point out that these cases of very early invasion have the histological appearance of a low-grade malignancy which can probably be cured by local excision.

TABLE III. TREATMENT OF 23 CASES OF EARLY INVASION

15 irradiated after diagnostic biopsy

8 treated by hysterectomy:

2 for other causes, the cervical carcinoma being incidental (1 subsequently irradiated also)

3 for supposed in situ carcinoma (1 subsequently irradiated)

3 for early invasive carcinoma

Pathological diagnoses in operative specimens in the last 3 were: a. in situ carcinoma

b. in situ carcinoma with gland invasion c. no remaining carcinoma

A review of the therapy employed in these 23 cases of early stromal invasion indicates that the view of this lesion as a still low-grade malignancy is not shared by most physicians treating these cases. In 15, or 65 per cent, the biopsy procedure, dilatation and curettage, or cone, was followed promptly by irradiation of some sort. In 2, the early invasive carcinoma was found in uteri removed for other causes (fibroids and endometriosis). One of these received post-operative irradiation by means of radium needles inserted in the cervical stump. The remaining 6 cases were treated by hysterectomy, but in 3 of these the earlier biopsy or cone had revealed only in situ carcinoma (with gland penetration in 2). When the early invasion was found by examination of the uterus, one of these 3 patients was given postoperative irradiation. In only 3 instances were hysterectomies performed as treatment, following removal of tissue which had shown very early invasion. These 3 uteri showed in situ carcinoma in one, in situ carcinoma with gland penetration in the second, and no remnant in the third. Table III summarizes these results.

The last case mentioned might indicate that these early invasive carcinomas, like cases of in situ carcinoma with gland penetration, might be eradicated by local excision. Not one of our cases was treated with local excision and follow-up Papanicolaou smears. We have the definite impression that most physicians who read of a microscopic focus of invasion in the pathology report of cervical tissue, immediately think of radium as the only form of treatment. The fact that many of these patients are quite young and the morbidity from radium treatment is not inconsiderable does not seem to alter this attitude.

Rationale for Local Excision and Follow-Up Smears

Certain psychological aspects of this problem cannot be overlooked. Anxiety on the part of both the gynecologist and his patient is sure to accompany knowledge of even the most superficial malignant invasion. The risk of radiation fibrosis involving the ureters or radiation necrosis involving the bowel can create justifiable apprehension when the lesion is one which should respond to surgical excision. Even a hysterectomy with a preliminary cone to rule out invasive carcinoma requires reliance on the gross appearance of the tissue and possibly frozen sections. Complete removal of the uterus leaves the physician without a satisfactory site for radium implantation should unqualified invasive carcinoma be discovered in the uterus after removal.

One can start with a positive Papanicolaou smear and follow it with an around-the-clock biopsy, a dilatation and curettage, and finally a deep cone; but if the most advanced lesion is still a miniature focus of early invasion well below the line of excision, the problem of therapy remains difficult. Conservative management consisting only of close observation has two points to recommend it. The first is the ease with which follow-up smears can be taken. The second is the evidence that invasive carcinoma takes a considerable length of time to develop. If the smears remain positive a few weeks after conization of early invasive carcinoma, it is still possible to choose the manner of treatment, whether it be irradiation, hysterectomy, or removal of more cervical tissue for biopsy. The short interval lost between the time of coning and the obtaining of positive smears, if tumor cells are left behind, should not materially hinder subsequent therapy. On the other hand, the patients who continue to have negative smears may be considered as cured by the cone, without the hazards of irradiation or hysterectomy. As long as cervical smears are reported negative by a competent cytologist, there is probably little need for undue apprehension.

This is a recommendation for more conservative management of a small group of patients showing early stromal invasion and representing 23 out of a series of 155 cases of epithelial neoplasia. It is based upon the employment of exfoliative cytological studies by experienced observers to reveal residual carcinoma promptly after local excision.

Individualizing each case is of great importance in clarifying the problem. There are some in situ lesions which appear so histologically malignant that the pathologist must regard them as likely to invade sooner than the ordinary case. Similarly, the gross appearance of the tissue can cause a great deal of concern to the surgeon, when the pathology report tells of a relatively benign condition. It is only in a conference between gynecologist and pathologist that these valuable individual impressions can be compared. It is in such conferences that many decisions concerning the management of these difficult cases can best be reached.

References

- 1. Carson, R. P., and Gall, E. A.: Am. J. Path. 30: 15, 1954.

- 1. Carson, R. P., and Gan, E. A.: Am. J. Fath. 30: 15, 1954.
 2. Fennell, R. H.: 8: 310, 1955.
 3. Younge, P. A.: Personal communication to Dr. Kenneth E. Cox.
 4. Fennell, R. H.: Cancer 8: 302, 1955.
 5. Hertig, A. T., and Younge, P. A.: Am. J. Obst. & Gynec. 64: 807, 1952.
 6. Wheeler, J. D., and Hertig, A. T.: Am. J. Clin. Path. 25: 345, 1955.

SURGERY AS AN ADJUNCT TO IRRADIATION THERAPY IN CARCINOMA OF THE CERVIX

Preliminary Report

EDWARD J. CRAWFORD, JR., M.D., LEWIS S. ROBINSON, M.D., AND LLOYD A. HORNBUCKLE, M.D., SHREVEPORT, LA.

(From the Gynecological Tumor Service of the Confederate Memorial Hospital)

THIS study was undertaken in an effort to evaluate the effect of radical hysterectomy and bilateral pelvic lymphadenectomy on Stage I and II cervical carcinoma that had been previously irradiated. Before an accurate evaluation of this type of surgery can be made, two important questions must be answered. First, can surgery be carried out post irradiation without unduly increasing the morbidity and mortality? Second, does radical surgery increase the survival rate of the previously irradiated carcinoma patient? If these two questions can be answered then the study will be worth while.

Material

From June, 1950, through December, 1954, 52 cases of Stage I and II cervical carcinoma were first given adequate irradiation therapy and then subjected to radical hysterectomy and bilateral pelvic lymphadenectomy. All of the clinical material, with the exception of one case, was derived through the Gynecological Tumor Service of the Confederate Memorial Hospital of Shreveport, Louisiana. Each patient received the preoperative irradiation, clinical investigation, and postoperative care in this institution.

Preoperative Study and Selection of Cases

Six weeks following the completion of irradiation each patient underwent an extensive investigation to determine her physical state and the response of the malignancy to irradiation. Each of the patients had quadrant biopsies of the cervix done six weeks post irradiation. Of the 52 patients biopsied, 5 had residual viable carcinoma. All patients had complete skeletal surveys for metastasis, electrocardiograms, nonprotein nitrogen determinations, proctoscopic examinations, and barium enemas. The urological workup included routine cystoscopy and intravenous pyelograms with retrograde pyelography when indicated.

In selection of the cases for operation all age groups were included. The only patients eliminated from the series were those felt to be poor surgical risks due to cardiovascular or renal disease.

Preoperative Irradiation

Each of these patients was treated preoperatively with a full therapeutic application of radium and x-ray. The Ernst applicator was used in each case with the individual dose varying between 6,400 and 7,200 mg. hr. X-ray therapy consisted of 2,000 r in air to 6 parts in 41 cases and 2,000 r in air to 4 parts in 11 cases.

All of the irradiation therapy was carried out by the Department of Radiology of the Confederate Memorial Hospital.

General Information

Age Distribution.—The ages of the patients in this group varied from 26 to 66 years. As is seen in Table I, the largest percentage (42 per cent) of patients fell into the decade between 31 and 40 years, the second largest group (29 per cent) in the decade between 41 and 50 years of age.

TABLE I. AGE DISTRIBUTION

AGE	NUMBER	%
21-30	3	6
31-40	. 22	42
41-50	15	29
51-60	10	19
31-40 41-50 51-60 61-70	2	4
Total	52	100

Race.—Even though the population of this hospital and its clinics is predominately Negro, there was a fairly equal distribution between the two races. There were 22 white and 30 Negro patients involved in this study.

Stage of Disease.—Prior to irradiation therapy each case was staged by a member of the Gynecological Tumor Clinic. The League of Nations classification was used to establish as much uniformity as possible between this and other series. Of the total 52 cases treated by irradiation and surgery, 27 were found to have Stage I and 25 to have Stage II cervical carcinoma.

Histologic Type of Carcinoma.—The type of malignancy in this series was distributed as follows: 48 cases of primary squamous-cell carcinoma of the cervix, 2 primary adenocarcinomas, and 2 squamous carcinomas of the cervical

Pregnancy.—Two patients with pregnancy and carcinoma of the cervix were treated in this institution during the past three years. One was treated with primary surgery, followed with radiation. This was a Stage I carcinoma and a pregnancy of seven weeks' gestation. The second patient had Stage II squamous carcinoma of the cervix complicating pregnancy at six and one-half months' gestation. A therapeutic abortion was done with subsequent radium, x-ray, and operation. Positive nodes were found in this patient at the time of operation and twelve months postoperatively a positive supraclavicular node was removed. The patient died sixteen months after operation with extensive metastases.

TABLE II. DURATION OF SURVIVAL FOLLOWING OPERATION

MONTHS	STAGE I	STAGE II	STAGES I AND I
0-6	2	3	5
7-12	0	0	0
13-18	3	2	5
19-24	3	. 0	3
25-30	6	. 7	13
31-36	2	1	3
37-42	4	2	6
43-48	3	3	6
49-54	0	2	2
Total	23	20	43

Results Following Surgery

Length of Survival (living with no evidence of disease).—Of the 52 patients, 43 (83 per cent) are living without evidence of recurrent disease from six to fifty-four months postoperatively. Eight patients have died since operation and one is living with recurrent disease.

Table II gives a breakdown as to the duration of survival postoperatively and the stage of the disease in these 43 cases.

Node Involvement and Residual Carcinoma in Cervix.—Lymph node metastasis was found in 5 of the 52 patients who underwent operation (9.6 per cent). In 8 additional patients, however, viable carcinoma was found in the cervix. One patient had both node involvement and residual carcinoma in the cervix. Thus, in a total of 13 patients (25 per cent) viable malignant tissue was removed surgically following therapeutic amounts of irradiation.

When lymph node metastasis was present, generally more than one node was involved. The obturator group of nodes was the most frequently involved. In two of the cervices residual carcinoma was found only in the blood vessels.

TABLE III. CASES WITH RESIDUAL CARCINOMA FOUND IN SURGICAL SPECIMENS

STAGE	NUMBER OF CASES	THOSE WITH POSITIVE NODES	%	THOSE WITH POSITIVE CERVIX	%
I	27	2	7.4	5	18
II	25	3	12	4	16

The presence of viable malignant cells in 9 of the cervices following therapeutic amounts of irradiation is rather difficult to explain. One would hardly expect to find this many cases of radioresistant carcinoma in such a small series of patients. However, each of these patients was operated upon within two to four months following the completion of irradiation therapy.

Survival Rate With Regard to Lymph Node Metastasis and Residual Disease in the Cervix.—Since this study involves a small number of patients no distinction is made as to the histological type of the lesion or to the lesions of the cervical stump. When Stages I and II are combined, 39 patients had negative nodes and cervices while 13 had either positive nodes or residual carcinoma in the cervix. Of the negative group 95 per cent are living without disease from six months to four and one-half years, while in the positive group 7, or 54 per cent, have survived over the same time interval.

Table IV shows that 4 deaths have resulted from recurrent disease: One from a pulmonary embolism on the twenty-fourth postoperative day; one from hepatic disease four years postoperatively; one from a cerebral vascular accident twenty-six months postoperatively; and one from intestinal obstruction two months postoperatively.

TABLE IV. SURVIVAL DATA

	STAGE I-27 CASES			STAGE II—25 CASES			STAGES I AND II-52 CASES					
	CER	S AND VIX ATIVE	CEF	S AND VIX TIVE	CEB	S AND VIX ATIVE	NODES CER POSI	VIX	CER	S AND VIX ATIVE	CE	S AND RVIX SITIVE
	NO.	%	NO.	1 %	NO.	1 %	NO.	%	NO.	1 %	NO.	1 %
Alive	19	90	5	83	18	100	2	29	37	95	7	54
Dead	2	10	1	17.	0	0	5	71	2	5	6	46
Total	21		6		18		7		39		13	
Surviving		89	0%			80	1%			84.	6%	

Primary Mortality.—Of the 52 patients operated upon, one died before leaving the hospital, a surgical mortality of 1.9 per cent. This patient died of a massive pulmonary embolism on the twentieth postoperative day.

Six other deaths occurred between two months to four years following operation. Table V shows the duration of survival, stage of disease, node involvement, and cause of death of the 8 patients who have died.

TABLE V. NUMBER OF PATIENTS WHO HAVE DIED SINCE OPERATION

CASE NUMBER	STAGE	NODE METASTASES	CERVIX		DURATION OF LIFE AFTER OPERATION	CAUSE OF DEATH
. 3	II	Rt. iliac Rt. obturator	Negative	26	months	Cerebral vascular accident. Post- mortem, No recur- rent disease
11	II	Negative	Residual cells in blood vessels	8	months	Metastatic carcinoma
27	I	Negative	Negative		days post-	Pulmonary embolus
28	II	Positive	Positive	2	months, 2 days	Intestinal obstruction
37	Ι	Negative	Negative		years	Death felt to be from hepatic disease. N postmortem
45	II	Negative	Positive. Lesion thought to be adequately ex- cised	15	months	Carcinoma
52	II	10 nodes posi- tive	Negative	22	months	Carcinoma
21	I	Positive	Negative	17	months	Recurrent carcinoma

Complications.—

Genitourinary complications: Urinary tract complications were by far the most common type in this series of cases. One patient (1.9 per cent) developed a vesicovaginal fistula which was present for some three and one-half years prior to repair. Surgical repair was finally permitted by this individual but an unsuccessful result was obtained.

Ureteral dilatation was demonstrated by intravenous pyelograms in 4 patients prior to operation and in a total of 14 (26.9 per cent) postoperatively. This figure represents the total number of patients with urinary tract complications. Ten (19.2 per cent) presented ureteral dilatation and/or hydronephrosis of varying degrees postoperatively that can be attributed directly to operation.

Seven of this group of patients (14 per cent) recovered spontaneously with no therapy. Of the remaining 7, all required therapy, ranging from ureteral dilatation to nephrostomy. Two nonfunctioning asymptomatic kidneys resulted. One patient died two months postoperatively with a large dilated ureter which was present prior to operation and decreased moderately in size postoperatively. Thus 7 cases presented urinary complications that necessitated therapy. Table VI shows the outcome of these cases.

Another urinary tract complication presented itself in this group of postoperative patients, this being the loss of bladder tone and residual urine. An
indwelling catheter was left in place routinely for seventy-two hours following
operation and the patients were catheterized for residual urine following the
first voiding. Thirty-eight patients (73 per cent) showed residual urine of less
than 100 c.c., while in fourteen (27 per cent) the residual was more than 100 c.c.
In this group it was necessary to replace the indwelling catheter for varying
periods of time, the shortest period being one day and the longest period being
three weeks. None of the patients continued to have residual urine after three
weeks.

TABLE VI. OUTCOME IN 14 CASES OF URETERAL DILATATION

N	CASE	PREOPERATIVE	POSTOPERATIVE	OUTCOME
2.	E. M. 51-33993 51-695	Bilateral hydro- nephrosis	Bilateral hydronephrosis, 2 months postopera- tively	Alive 32 months postoperatively Intravenous pyelogram 3 months following surgery showed no change. Patient asymptomatic Spontaneous regression
10.	L. B. 52-44610 54-302		Left hydronephrosis	Alive 3 months postoperatively. Negative intravenous pyelogram 3 months postoperatively. Spon- taneous regression
15.	R. D. 53-55036 53-083		Same, with pressure defect	Alive 17 months postoperatively Dilatation has decreased con- siderably since operation. Pa- tient is asymptomatic
16.	F. H. 53-55650 53-105	Negative	Slight dilatation right ureter	Alive 17 months postoperatively. No therapy. Patient now has negative intravenous pyelogram
20.	E. C. 54-75642 54-475	Negative	Right hydronephrosis	Alive 2 months postoperatively. Responding to ureteral dilata- tions
49.	L. W. 50-12783 50-734	Negative	Bilateral hydronephrosis	Alive 47 months postoperatively. Vesicovaginal fistula. Nonfunc- tioning right kidney, asympto- matic. Surgical repair unsuc- cessful
50.	M. J. 50-12176 50-774	Negative	Left hydronephrosis and ureteral stricture	Alive 46 months postoperatively. Nephrostomy eighth postopera- tive day, nonfunctioning asymp- tomatic left kidney
52.	A. S. 50-17629	Negative	Bilateral hydronephrosis	Died 24 months postoperatively with recurrent disease
17.	J. P. 54-7324 54-326	Negative	Right hydronephrosis and hydroureter, 6 weeks postoperatively	Alive 4 months. Marked improvement at 4 months with only slight dilatation of ureter
25.	O. C. 53-53724 53-004	Negative	Dilatation of pelvis and calyces, left	Alive 17 months. Normal intra- venous pyelogram 6 months post- operatively
30.	M. S. 52-43624 52-505	Negative		Alive 25 months postoperatively. Patient is asymptomatic
	B. A. 51-31322 52-789	Negative	Right lower ureter not visualized	Alive with recurrence 20 months postoperatively; right ureter cut during operation, reanastomosed, stricture dilated with good re-
28.	M. S. 54-72623	Large hydroureter with mass ob- struction at level of cervix	Some decrease in size postoperatively	sults Died 2 months postoperatively of intestinal obstruction and anuria
34.	R. S. 101424	Negative	Right hydronephrosis with ureteral stricture	Alive 28 months postoperatively. Ureter dilated for period of 6 months. Good response. Now has normal intravenous pyelo- gram

Complications other than genitourinary: Two patients had severe hemorrhages at the time of operation, one so severe that it was necessary to discontinue the operation and complete the procedure at a later date. One patient died of a massive pulmonary embolus postoperatively. Another patient developed a hematoma in the left lower quadrant which responded to conservative therapy. Still another had rectal bleeding and three developed incomplete rectal strictures, all of which responded to dilatation.

Summary and Conclusions

This study is based on 52 cases of Stage I and Stage II carcinoma of the cervix that were first irradiated and then subjected to radical hysterectomy with pelvic lymphadenectomy. The series was begun in June of 1950 and extends through December of 1954.

Of this group 27 were found to have Stage I disease and 25 Stage II. There were 48 cases of primary squamous carcinoma, and 2 cases each of adenocarcinoma and squamous carcinoma of the cervical stump.

Forty-three patients, 85 per cent of this group, are alive, without evidence of recurrence, from six to fifty-four months, 8 have died, and one is alive with recurrent disease.

The primary operative mortality was 1.9 per cent. Nineteen per cent presented postoperative urinary tract complications, with only one fistula, which was vesicovaginal in location.

At the present time this series is too small and the patients have not been followed over a long enough time interval to evaluate the effects of operation on previously irradiated cervical carcinoma. It is our feeling, however, that radical surgery can be carried out in the previously irradiated patient without markedly increasing the mortality and postoperative complications. If this type of surgery increases the survival rate in Stage I and II cervical carcinoma after irradiation, it will then be justified.

We wish to express our appreciation of the cooperation of the Department of Radiology of the Confederate Memorial Hospital.

PRIMARY CARCINOMA OF THE FALLOPIAN TUBE

ARTHUR N. FRANKEL, M.D., NEW YORK, N. Y.

(From the Gynecological Services of Beth Israel and Harlem Hospitals)

PRIMARY carcinoma of the Fallopian tubes was first described by Orthmann¹ in 1888. Nearly 600 cases have been reported to date.² Ten cases of primary carcinoma of the Fallopian tube were seen from 1942 to 1951, 7 at Beth Israel Hospital and 3 at Harlem Hospital, these forming the basis of the present report.

During this 10 year period there were 435 cases of cancer of the genital tract at Beth Israel Hospital, 7 of which were primary carcinoma of the Fallopian tube, an incidence of 1.6 per cent, and 687 cases of cancer of the genital tract at Harlem Hospital, 3 of which were primary carcinoma of the Fallopian tube, an incidence of 0.43 per cent. Lofgren and Dockerty,³ in a report of 16 cases, had an incidence of 0.16 per cent, Emge,⁴ in a report of 6 cases, had an incidence of 0.3 per cent, and Hu and associates,⁵ in a report of 12 cases, had an incidence of 0.31 per cent. Reports vary from 0.1 to 0.5 per cent, averaging 0.3 per cent, according to Corscaden.⁶ The high percentage incidence at Beth Israel Hospital may be explained by the low incidence of carcinoma of the cervix at the institution whose patients are predominantly of the Jewish race.

The important clinical and pathological data on these ten cases are summarized in the accompanying table (Table I).

Age Incidence

The average age was 49, with extremes of 38 and 61 years. Lofgren found the average age to be 50.9, with extremes of 34 and 65 years. In the report of Stern and Hanley,⁷ the average age was 46, with extremes of 34 and 64 years. Hu and associates quoted 3 cases in the literature at 18 years of age. Fullerton's⁸ oldest patient was 80 years of age. The average age is, according to Wechsler,⁹ almost a decade earlier than the age in cases of fundal carcinoma.

Symptoms

The most common complaints in our series were: (1) vaginal discharge or bleeding, (2) lower abdominal pain, and (3) enlargement of the abdomen. Vaginal discharge was present in 6 of the cases, from mucoid to serosanguineous in one case, and with frank bleeding in 5 cases. Two of the 5 were postmenopausal and the bleeding was constant; 3 had menorrhagia associated with fibroids. The duration of the discharge varied from 2 months to 3 years. Vaginal discharge or bleeding was present in 10 of 16 cases in Lofgren's series, in 5 of 6 of Emge's, and in 10 of 12 cases of Hu's.

Pain was a complaint in as many cases as vaginal bleeding or discharge (6 of the 10 cases). The pain was lower abdominal and unilateral, on the same side as the lesion, in 3 of the 4 cases in which the involvement was unilateral.

TABLE I. SUMMARY

OF CAS

INVOL (APAR Bilater

Right

Right

Right

Right

Left t

Left t

Bilate Broad men tasi

Left Mesos met

Right

CASE	NAME OF PATIENT	AGE	RACE	GRAVIDITY	COMPLAINTS	PREOPERATIVE DIAGNOSI
1	A. R. Private Beth Israel	43	White	Para i Gravida ii	Vaginal discharge—(sero- sanguineous) Abdominal pain	Fibroid uterus Adnexal disease Malignancy of uterus or adnexa ??
2	M. L. Private Beth Israel	58	White	Para iii Gravida v	Uterine bleeding—2 months (postmenopausal)	Endometrial hyperplasi (suggestive of malignancy)
3	E. L.* Service Beth Israel	61	White	Para i Gravida ii	Uterine bleeding—3 years Abdominal pain—1 week Loss of weight— 20 pounds in 1 year	Ovarian tumor
4	E. S. Service Harlem	38	Negro	Para 0 Gravida 0	Uterine bleeding—2 months (menorrhagia) Abdominal mass—6 months	Fibroid uterus
5	L. B. S. Service Harlem	45	Negro	Para 0 Gravida 0	Abdominal mass—3 months Uterine bleeding—2 months (menorrhagia) Abdominal pain Temperature 104° F.	Left tuboovarian abscess Right pyosalpinx
					Chills Frequency of urination Dysuria	
6	D. R. Service Harlem	40	Negro	Para 0 Gravida 0	Abdominal mass—2 years Abdominal pain—1 year Uterine bleeding—2 years (menorrhagia)	Left tuboovarian abscess Left pyosalpinx
7	E. W. Private Beth Israel	45	White	Para 0 Gravida 0	Uterine bleeding—2 weeks (menorrhagia)	Fibroid uterus
8	P. S. Service Beth Israel	54	White	Para ii Gravida v	Pelvic discomfort Frequency of urination } 6 Dysuria } months	Fibroid uterus
9	M. S. Service Beth Israel	51	White	Para iv Gravida v	Abdominal pain Chills Temperature 104° F. $\begin{cases} 1 \\ \text{day} \end{cases}$	Bilateral tuboovarian disease
10	M. S.* Private Beth Israel	53	White	Para iii Gravida iii	Abdominal mass Loss of weight	Fibroid uterus

^{*}E. L. (Case 3) and M. S. (Case 10) were previously reported by Drs. Morton Vesell and Ham Schneider. 15

MARY OF CASE HISTORIES

	(AT (APAROTOMY)	OPERATION	X-RAY THERAPY	PATHOLOGY	METASTASIS OR RECURRENCE	SURVIVAL
B	ilateral, tubes	Total abdominal hysterectomy Bilateral salpingo- oophorectomy	Yes	Papillary adeno- carcinoma (bilateral)	No record	No record
Ri	ight tube	Total abdominal hysterectomy Bilateral salpingo- oophorectomy	Yes	Papillary carcinoma	None	3½ years (living)
R	ight tube	Total abdominal hysterectomy Bilateral salpingo- oophorectomy	Yes	Necrotizing adeno- carcinoma	Pelvic and vaginal	20 months
R	ight tube	Supracervical hysterectomy Bilateral salpingo- oophorectomy Appendectomy		Papillary adeno- carcinoma	Liver	4½ years
R	ight tube	Total abdominal hysterectomy Bilateral salpingo- oophorectomy	Yes	Papillary adeno- carcinoma	Pelvic	2½ years
ı						
L	eft tube	Supracervical hysterectomy Bilateral salpingo- oophorectomy	Yes	Adenocarcinoma		8 years
L	eft tube	Supracervical hysterectomy Bilateral salpingo- oophorectomy		Adenocarcinoma	No record	No record
	Broad liga-	Supracervical hysterectomy Bilateral salpingo- oophorectomy		Partly papillary and partly solid carcinoma	Vagina	4 years
	eft tube desosalpinx metastasis	Salpingo-oophorectomy, left		Partly papillary and partly solid carcinoma	Pelvic and vaginal	2 years
H	Right tube	Total abdominal hysterectomy Bilateral salpingo- oophorectomy	Yes	Anaplastic solid papillary car- cinoma	Vaginal vault and vagina	15 months

The duration of the pain was from 2 days to 2 years. In 3 cases it was acute (2 days to a week before admission to the hospital). Pain was the chief complaint in 50 per cent of the cases reported by Hu and associates and Lofgren, and was noted to be usually on the side of the tubal involvement.

Enlargement of the lower abdomen was noticed by 4 of the patients in this series. It was found in 3 of Lofgren's 16 cases, in 2 of Emge's 6, and in 3 of Hu's 12. It had been present from 3 months to 15 years and in 2 of the

cases was associated with fibromyomas.



Fig. 1.—Case 1. Papillary adenocarcinoma. (×50.)

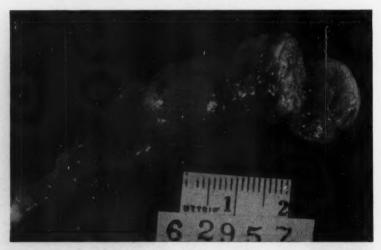


Fig. 2.—Case 2. Cross section of Fallopian tube. Note characteristic distention of distal portion.

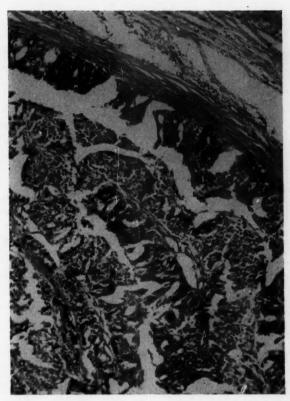


Fig. 3.—Case 2. Papillary adenocarcinoma (wall not invaded). $(\times 50.)$



Fig. 4.—Case 3. Necrotizing adenocarcinoma. (×20.)

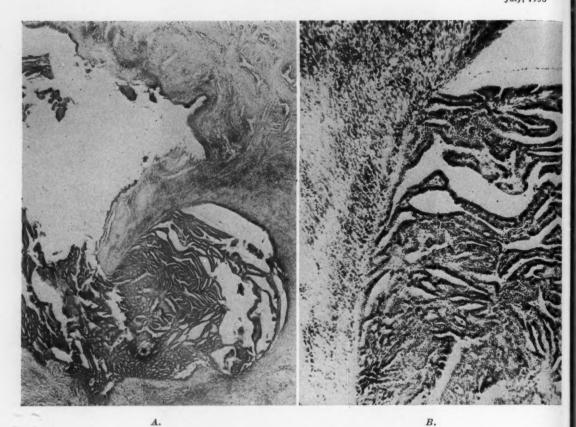


Fig. 5.—Case 4. A, Papillary adenocarcinoma of Fallopian tube. $(\times 10.)$ B, Papillary adenocarcinoma. $(\times 75.)$

The symptoms of vaginal discharge or bleeding, abdominal pain, and swelling of the abdomen are recognized as a common triad by all authors on this subject.

The phenomenon of hydrops tubae profluens, which has been mentioned by Anspach¹⁰ as occurring fairly frequently in primary carcinoma of the Fallopian tube, had not been observed in this series. The other symptoms were a combination of frequency and dysuria found in 4 patients and a substantial loss of weight in 2. Sterility is associated with primary carcinoma of the Fallopian tube; it was found in 2 per cent of Hu's series, in 44 per cent of Sanger and Barth's,¹¹ and in 32 per cent of Curtis';¹² it was found in 3 of our series, 30 per cent.

Physical Findings

In none of our cases was a preoperative diagnosis of carcinoma of the Fallopian tube made. In one a diagnosis of endometrial carcinoma of the uterus was made, based on curettings reported as suspicious of malignancy. A preoperative diagnosis of fibroid uterus was made in 4 cases, ovarian malignancy in one, bilateral tuboovarian disease in 2 cases, a combination of right tuboovarian abscess, fibroid uterus, and left pyosalpinx in one. In one case, a Papanicolaou smear was done with a report, "suspicious of malignancy." The patient was operated on with a preoperative diagnosis of fibroid uterus and adnexal disease, with a questionable malignancy of the uterus or adnexa. Therefore, in only 3 cases was pelvic malignancy even suspected, one based on

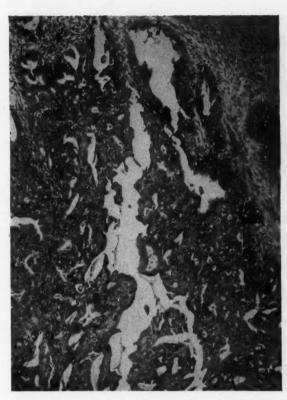


Fig. 6.—Case 5. Papillary adenocarcinoma invading wall. (\times 50.)

no-



Fig. 7.—Case 6. Adenocarcinoma. $(\times 70.)$



Fig. 8.—Case 7. Adenocarcinoma with invasion of muscularis. $(\times 20.)$

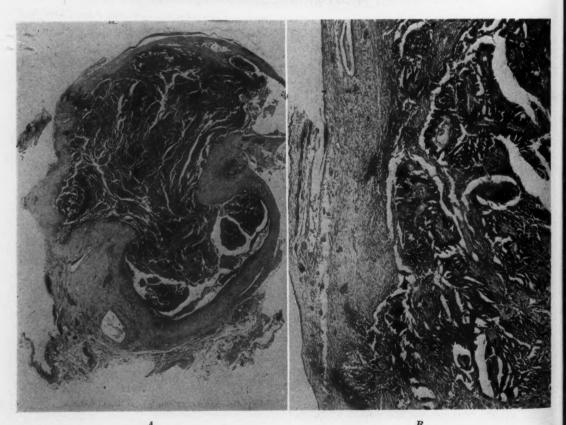


Fig. 9.—Case 8. A, Partly papillary and partly "solid" carcinoma of Fallopian tube. $(\times 5.)$ B, Papillary carcinoma showing invasion of muscularis. $(\times 20.)$

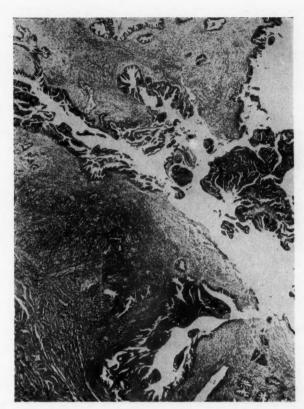


Fig. 10.—Case 9. Partly papillary and partly "solid" carcinoma with invasion of wall. $(\times 20.)$



Fig. 11.—Case 10. Anaplastic carcinoma. (×50.)

a suspicious curettage, another on a fixed postmenopausal mass in the fornix, and the third on a suspicious Papanicolaou smear. A preoperative diagnosis of primary carcinoma of the Fallopian tube is rarely made.

Surgical Findings

In only one of the cases presented was a diagnosis made at laparotomy. The others were discovered microscopically in the laboratory. In 6 of the cases the involved tubes were distended, usually at the distal ends. The condition resembled a pyosalpinx, hydrosalpinx, or hematosalpinx. Four of the cases resembled tuboovarian inflammatory masses, with adhesions to the uterus, sigmoid, and cul-de-sac. None of the patients had ascites or implants on the pelvic viscera to suggest malignancy. Hu and associates reported the incidence of ascites to be as high as 10 per cent in the literature.

Pathological Data

Gross: Unilateral involvement was found in 8 of the 10 cases, with the right tube involved in 5, and the left 3 times. Bilateral involvement was present twice. Corscaden says the lesion is usually unilateral and usually on the right side, with no explanation for it. Emge's series showed 70 per cent of his cases to be unilateral and Lofgren reported bilateral lesions occurring in 25 per cent of the cases reported in the literature.

The size of the lesion varied from 1.25 to 7.5 cm. in diameter and from 5 to 17.5 cm, in length. The size of the larger lesions seemed to be augmented by an associated hemato- or hydrosalpinx. All but 2 were encapsulated, one was a solid carcinoma with tuboovarian adhesions, and the other was a carcinoma of the tube invading the broad ligament. The distal portion of the tube was generally the most distended. Hematosalpinx was associated in 6 of the tubes, hydrosalpinx in one, and pyosalpinx in 3. In the remainder, the tubal distention was due primarily to the proliferating carcinoma tissue. The tissue was grossly papillary in 3 of the involved tubes; where no gross architectural tissue pattern was present, the tube was distended with a friable, gray, brownish-yellow, soft, and frequently purulent and necrotic tissue. Uninvolved portions of the tube were at times thickened and inflamed. Evidence of subacute or chronic salpingitis was present in the contralateral tubes in 5 cases, excluding the 2 contralateral malignant involvements. Watkins and Wilson, 13 Lofgren, and others have pointed to the close association between tubal carcinomatous and inflammatory lesions. Lofgren, in his series, found 100 per cent incidence of subacute or chronic inflammation in the uninvolved portions of the carcinomatous tubes.

Associated pathological conditions consisted of 4 cases of fibromyomas, 3 simple ovarian cysts, 2 tuboovarian abscesses, and 1 hydrosalpinx. There were no malignant implants or metastases at the time of the first laparotomy, except for one case of solid carcinomatous lesions found in tuboovarian adhesions, and in another metastases to the broad ligament and contralateral tube.

Microscopically, the lesion in the involved tube was papillary carcinoma in 5, partly papillary and partly solid in 2, adenomatous in 2, anaplastic in 1, and necrotizing in 1.

End Result of Treatment

The treatment recommended by most authors is panhysterectomy and bilateral salpingo-oophorectomy followed by radiation; they also recommend palliative radiation when extensive invasion of a neighboring viscus has taken place.

Five of the patients had total abdominal hysterectomies and bilateral salpingo-oophorectomies, 4 had supracervical hysterectomies and bilateral salpingo-oophorectomies. In one case a left salpingo-oophorectomy was performed, with vaginal draining for a pelvic abscess, the right adnexa being not found at the time of the operation. In 4 of the 10 cases there were records of radiation therapy following operation. Radiation showed no appreciable effect in our series on increasing the salvage rate as compared to that of patients who did not receive radiation. Our 5 year survival rate was 10 per cent as only one patient has passed the 5 year mark, although another is well 31/2 years postoperatively. None of Emge's patients lived over 20 months; Hu and his collaborators reported a 40 per cent cure, and Lofgren a 16 per cent cure. In 2 of our cases, no record of any follow-up can be found. One lived 8 years following a supracervical hysterectomy and bilateral salpingo-oophorectomy, and when last heard of was in a city hospital for carcinoma of the cervix. One is known to be living and well $3\frac{1}{2}$ years following operation. Two others lived approximately 4 years. In one, the lesion metastasized to the liver and in the other to the anterior vaginal wall. Another died 21/2 years after the occurrence of pelvic metastases. One lived about 2 years and when last seen was receiving radiation therapy for pelvic metastases. Another, after approximately 20 months, when last seen had pelvic and vaginal metastases. One developed metastases to the vaginal vault and vagina and died 15 months following operation.

Comment

The early clinical recognition of primary carcinoma of the Fallopian tube is difficult since there are no specific symptoms and the lesion is frequently masked by associated pathological conditions such as fibromyomas of the uterus, pelvic inflammatory disease, and ovarian neoplasm. Papanicolaou vaginal smears, if used routinely for vaginal discharges, may be of value. Corscaden reported a case of primary carcinoma of the Fallopian tube in which the diagnosis was made by a positive Papanicolaou vaginal smear and he is of the belief that more cases will be diagnosed with the help of this test. A case of Dr. Henry C. Falk's of secondary carcinoma of the Fallopian tube with a primary ovarian malignancy is mentioned to bear out this fact, as a laparotomy was performed on the basis of a positive Papanicolaou vaginal smear. Yo Seup Song14 also reports a case of primary carcinoma of the Fallopian tube, the diagnosis of which was made on the basis of routine Papanicolaou vaginal smears 4 hours post mortem. The smears were examined before completion of necropsy, which showed a primary adenocarcinoma of the Fallopian This diagnosis had not been suspected during life. The author feels that hysterosalpingography as a diagnostic procedure after a positive smear is dangerous on account of the possibility of disseminating the cancer. Culdoscopy may be an adjuvant in diagnosis although it had not been used in this series. Its value is questionable since the diagnosis could not be made at laparotomy in 9 of the 10 cases. Failure to demonstrate cervical or endometrial carcinoma in the presence of a positive Papanicolaou smear calls for exhaustive search for pelvic malignancy. Surgical exploration should be performed: (1) at and after the menopausal age when an obscure pelvic mass presents itself, (2) when the symptoms of lower abdominal pain, vaginal discharge or bleeding, and a lateral pelvic mass are present at and after the menopausal age, and (3) when inflammatory manifestations are present at or after the menopausal age when inflammatory conditions are rare. Every pelvic organ removed should be examined at the operating table so that complete surgery can be performed if malignancy is found.

Summary

- 1. Ten cases of primary carcinoma of the Fallopian tube are presented.
- 2. The disease is difficult to diagnose.
- 3. Papanicolaou vaginal smears used routinely for vaginal discharge or bleeding may be an aid to early diagnosis provided the isthmic portion of the tube is patent.
- 4. The low salvage rate might be raised: (a) if the clinician were cognizant of the possibility of primary carcinoma of the Fallopian tube; (b) if Papanicolaou vaginal smears were used routinely for vaginal discharge or bleeding; and (c) if an exploratory laparotomy were performed for all adnexal masses which after careful investigation cannot be accurately diagnosed or the diagnosis is still in doubt.

Grateful acknowledgment is made to Dr. Henry C. Falk, Director of Obstetrics and Gynecology at Beth Israel Hospital, for his aid in the preparation of this paper, to Dr. David H. Dreizin, Associate Attending Pathologist at Beth Israel Hospital, for the preparation of the photomicrographs for this study, and to Dr. M. Leo Bobrow, Director of Gynecology at Harlem Hospital, for his generous cooperation.

References

- 1. Orthmann: Ztschr. Geburtsh. u. Gynäk. 15: 212, 1888.
- Orthmann: Ztschr. Geburtsh. u. Gynäk. 15: 212, 1888.
 Kimbrough, R. A., and Bruce, C. C.: In Davis, Carl Henry, editor: Gynecology and Obstetrics, Hagerstown, Maryland, 1953, W. F. Prior Co., Inc., vol. 11, chap. 14, p. 12.
 Lofgren, K. A., and Dockerty, M. B.: Surg., Gynec. & Obst. 82: 199, 1946.
 Emge, L. A.: West. J. Surg. 56: 334, 1948.
 Hu, M. L., Taymor, M. D., and Hertig, A. F.: Am. J. Obst. & Gynec. 59: 58, 1950.
 Corscaden, J. A.: Gynecological Cancer, New York, 1951, Thomas Nelson & Sons, p. 284.
 Stern, B. D., and Hanley, B. J.: Am. J. Obst. & Gynec. 58: 517, 1949.
 Fullerton, W. D.: Am. J. Obst. & Gynec. 48: 467, 1940.
 Wechsler, H. F.: Arch. Path. & Lab. Med. 2: 161, 1926.
 Anspach, B. M.: Am. J. Obst. & Gynec. 20: 511, 1930.

- 10. Anspach, B. M.: Am. J. OBST. & GYNEC. 20: 511, 1930.
- Alaspach, B. M.: AM. J. Obst. & Gynec. 20, 311, 1950.
 Sanger, M., and Barth, J.: Cited from Halban, J., and Seitz, L.: Biologie und Pathologie des Weibes, Berlin, 1926, Urban & Schwarzenberg, Band V, 1. Teil, 13.
 Curtis, A. H., editor: Obstetrics & Gynecology, Philadelphia, 1953, W. B. Saunders Company, vol. 2, p. 1042.
 Watkins, R. E., and Wilson, W. M.: Surg., Gynec. & Obst. 51: 125, 1930.
- 14. Song, Yo Seup: Am. J. OBST. & GYNEC. 70: 29, 1955.
- 15. Vesell, Morton, and Schneider, Harry: Am. J. OBST. & GYNEC. 54: 140, 1947.

OVARIAN TUMORS AND ABNORMAL UTERINE BLEEDING*

MELVYN A. BAYLY, M.D., AND R. R. GREENE, M.D., CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology of Northwestern University Medical School, and of the Chicago Wesley Memorial Hospital, and from the Chicago Maternity Center)

IN MOST textbooks, articles, or discussions, "ovarian tumors" are listed among the various causes of abnormal uterine bleeding. In some instances hormone-producing ovarian tumors do cause abnormal uterine bleeding; however, we doubt that the non-hormone-producing tumors have any such effect.

In 1949 we¹ studied a series of 74 non-hormone-producing tumors together with accompanying uteri. Only 15 of these patients had had abnormal uterine bleeding. In all but 3, "causes" for this bleeding other than the ovarian tumor were believed to be present. After reviewing these data, we now believe an additional case (No. 6 of our previous report) should be included in the "unexplained" group. This patient had residues of pelvic inflammatory disease, and we now have evidence which makes us doubt that this condition causes abnormal uterine bleeding.² The corrected data then are: 15 (20 per cent) of 74 patients with ovarian tumors had abnormal uterine bleeding. In all but 4 (5.4 per cent) there were "causes" for the bleeding, other than the ovarian tumor.

Our first series was admittedly small and that report has been almost universally ignored, even in our own institution. It was therefore decided to reopen the subject by studying the cases accumulated since 1949.

The pertinent literature prior to 1949 was reviewed in our previous article and will not be repeated here. Subsequently several studies concerning ovarian tumors have directly or indirectly touched on this problem. Allan and Hertig³ studied a group of ovarian carcinomas and decided that abnormal uterine bleeding was not a characteristic symptom since it was found in only 18.5 per cent of their patients. Pearse and Behrman⁴ studied another group of ovarian malignancies and found "no significant abnormalities" as far as bleeding was concerned. On the other hand, J. Mathieu⁵ hypothesized that abnormal uterine bleeding might be caused by coexisting ovarian tumors. Several theories were advanced. Meigs⁶ recently reviewed a group of benign and malignant ovarian tumors other than fibromas associated with ascites and hydrothorax. In scanning the tables presented, it was noted that only 3 instances of abnormal uterine bleeding were listed in the 40 cases. Way¹ described a series of 130 ovarian malignancies and found only 9 instances of abnormal bleeding.

^{*}Financed in part by a cancer control grant from the National Cancer Institute of the Department of Health, Education, and Welfare.

Materials and Methods

Since 1949 tissues from 80 non-hormone-producing ovarian tumors and the accompanying uteri were prepared in the laboratory of the Department of Obstetrics and Gynecology of Northwestern University Medical School. Many other ovarian tumors removed during that time were not included because the uterus was not removed. Just as a matter of curiosity, however, a consecutive series of non-hormone-producing tumors which were removed without the uteri was checked and the interesting results will be discussed later.

The types of ovarian tumors encountered in this series are listed in Table I. The figures in parentheses indicate the number of tumors reported previously.

TABLE I. TYPES OF OVARIAN TUMORS INCLUDED IN PRESENT SERIES

Pseudomucinous cystadenomas	9 (9)
With serous cystadenoma	1
With fibroma	1
With Brenner tumor	1
Serous cystadenomas	15 (18)
With fibroma	1
Serous cystomas	15 (5)
Benign teratoids	17 (17)
With Brenner tumor	1 .
Fibromas and fibroadenomas	9 (7)
Carcinomas	12 (18)
Brenner tumors (alone)	3

In a review of the patients' records, the following were considered to be abnormal: intermenstrual bleeding or spotting (postcoital in 3); increase in the amount and/or the length of menstrual flow; decrease in the interval to 21 days or less; and postmenopausal bleeding (12 or more months post menopause).

Results

Abnormal uterine bleeding was noted in the histories of 23 of the 80 patients (29 per cent). Seventeen of these 23 instances were easily explained by coexisting pathologic conditions as follows: submucous fibroids, 9; acute cervicitis in one instance which caused postcoital spotting; hemorrhagic endometrial polyps, 3; endometrial carcinoma, 2; hemorrhagic endocervical polyps, which caused spotting, 2. The remaining 6 cases merit more detailed comment.

CASE 1.—A 37-year-old woman complained for the last year of a variable cyclic interval of 10 to 20 days with 4 days' duration. The bleeding was not excessive. The pathologic findings included a benign cystic teratoma of the ovary, and endometriosis of the rectum and uterosacral ligaments. The endometrium was secretory, and there was a corpus luteum in the normal ovary. What the tumor-bleeding relationship would be is conjectural. There seems to be no obvious cause, and the history of abnormal bleeding has not been explained.

CASE 2.—A 26-year-old patient complained of an irregular menstrual interval of 18 to 30 days for one year with a duration of five days; the periods were not excessive. The pathologic findings included a papillary serous cystadenoma of the left ovary, subserous and intramural fibroids with hyaline degeneration, adenomyosis, and a right hydrosalpinx. The endometrium was normal and in the proliferative phase. Although there were many pathologic changes, nothing explained the unpredictable and abnormal menstrual interval.

CASE 3.—A 46-year-old woman described a gradual increase in menstrual flow for 3 months. A similar episode several months previously was followed by a dilatation and curet-

tage; the tissue obtained was normal. The patient had received estrogens until 3 months before, but had had none since. The findings included a benign cystic teratoma, intramural fibroids, adenomyosis, and proliferative endometrium. This change in the bleeding pattern was apparently not explained by coexisting pathologic conditions.

Case 4.—A 42-year-old patient complained of intermenstrual spotting and gushing bleeding for at least 60 days. On admission to the hospital the red blood count was 4.37 million and hemoglobin 12.7 Gm. The findings included intramural fibroids 4 to 5 cm. in diameter, a benign cystic teratoma, and a small Brenner tumor. The endometrium was secretory. One might doubt that bleeding had been excessive with such blood counts, but there is no obvious reason for the spotting. This case is unexplained.

CASE 5.—A 53-year-old woman complained of daily vaginal bleeding for 30 days. The findings included subserous and intramural fibroids, a pseudomucinous cystadenoma 18 cm. in diameter, and extensive adenomyosis. The endometrium was secretory. Whether or not any of the pathologic findings caused the abnormal bleeding is unknown. This case is listed as unexplained.

CASE 6.—A 37-year-old woman complained of continuous vaginal spotting for 15 days and postcoital spotting for one year. The cervix was normal. There was a serous cystadenoma of the left ovary, 15 cm. in diameter, with an endometrioma of the right ovary, subserous and intramural fibroids, adenomyosis, and secretory endometrium. Once again there are many abnormalities, but just what caused the bleeding is not clear. This too is listed as unknown.

These 6 cases of abnormal uterine bleeding are difficult to evaluate. There are abundant pathologic changes; yet none seems to be the real cause of abnormal bleeding. Of the 6 unexplained cases, there were adenomyosis in 4 and intramural and subserous fibroids in 5. Although many might consider some of these entities, particularly adenomyosis, as a cause of abnormal bleeding, there is no good evidence at this time to substantiate that this was true in our cases.

As a matter of interest, the histories were reviewed of a group of 36 consecutive patients from whom ovarian tumors had been removed, but not the uterus. This group was comprised of women who were younger but had the same ovarian tumors (excluding carcinomas) as the group with hysterectomy. In the 36 histories only 3 instances of abnormal bleeding were recorded! These data would suggest that advancing years are more important than the ovarian tumors as a factor in abnormal bleeding. A similar phenomenon has been noted by us in relation to abnormal bleeding associated with endometriosis.³

Comment

Eighty cases of non-hormone-producing tumors of the ovary and accompanying uteri have been studied. Of the 23 instances where uterine bleeding was abnormal, 6, or 7.5 per cent, were not satisfactorily explained by the generous amount of coexisting pathologic findings which were present. There is reason to doubt whether one or two of these should be placed in the category of abnormal bleeding; nevertheless, they were so labeled. Adding to these the 74 presented in 1949 gives a total of 154 cases. Abnormal bleeding was present in 38 but was believed to be caused by coexisting pathologic changes in the uterus in 28. Only in the remaining 10 of the 154 (6.5 per cent) could the tumor be considered as a possible "cause" of the bleeding.

It seems to us that if non-hormone-producing ovarian tumors actually constitute an important cause of abnormal uterine bleeding, the incidence would

be a great deal higher. We also believe, therefore, that it is high time that we cease believing and teaching that there is a mysterious causal relationship between these tumors and abnormal uterine bleeding.

References

- Bayly, M. A., and Greene, R. R.: Am. J. Obst. & Gynec. 57: 984, 1949.
 Bayly, M. A., and Gatlin, A.: Unpublished data.
 Allan, Malcolm S., and Hertig, Arthur: Am. J. Obst. & Gynec. 58: 640, 1949.
 Pearse, Warren H., and Behrman, S. J.: Obst. & Gynec. 3: 32, 1954.
 Mathieu, J.: Rev. franç. gynéc. et obst. 43: 85, 1948.
 Meigs, J. V.: Obst. & Gynec. 3: 471, 1954.
 Way, Stanley: Malignant Disease of the Genital Tract, Philadelphia, 1951, The Blakiston Company.
 Bayly, M. A., and Gossack, Larry L.: Am. J. Obst. & Gynec. 72: 147, 1956.
- 8. Bayly, M. A., and Gossack, Larry L.: Am. J. OBST. & GYNEC. 72: 147, 1956.

EXTERNAL ENDOMETRIOSIS AND ABNORMAL UTERINE BLEEDING*

MELVYN A. BAYLY, M.D., AND LARRY L. GOSSACK, M.D., CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology, Northwestern University Medical School and Chicago Wesley Memorial Hospital)

T IS a common belief and usual teaching that external endometriosis is frequently the cause of abnormal uterine bleeding. Counseller reported some menstrual abnormality in 88 per cent of 1,342 patients operated upon. Payne² found either prolonged or excessive bleeding in 56 per cent of his patients operated upon; while Lamb³ found abnormal bleeding in 46 per cent. In Bookrajian and Morrow's series there was abnormal bleeding in 47 per cent of the patients. Drevfuss⁵ found that 92 of 138 patients with endometriosis complained of abnormal bleeding. Preston and Campbell9 indicated that 40 per cent of their patients had abnormal bleeding, while in numerous other series, the incidence ranged from 20 per cent up.6-9 Not everyone has been so willing to blame endometriosis for various types of abnormal bleeding. Te Linde and Scott¹⁰ believed that the role of endometriosis in abnormal bleeding is overemphasized and estimated that the true percentage would correctly be about 15 to 20 per cent. In many of these reports the criteria for abnormal bleeding were omitted. This makes evaluation difficult and may explain in part, at least, the great variation in these statistics. On the other hand Randall¹¹ has suggested that conditions other than the endometriosis might be to blame. Beecham¹² wondered if coexisting pathological states might not be the most likely cause of bleeding.

As part of a larger study on the various causes of abnormal uterine bleeding, we have investigated the relationship of external endometriosis and abnormal uterine bleeding.

Method and Materials

From March 1, 1949, until Dec. 31, 1952, 1,177 laparotomies were performed by the gynecologists of the Chicago Wesley Memorial Hospital. During this period each abdomen opened was carefully inspected, and whenever endometriosis was diagnosed grossly a detailed description of such findings was recorded. For this series, only those cases were included where all tissues including the uterus were available for histological study. As is the custom on our service, the specimens were first sent to the general laboratory of the hospital and blocks for routine sections were cut; the remaining tissue was taken to the Northwestern Gynecological Pathology Laboratory where further blocks were made.

The problem of what constitutes abnormal bleeding was resolved by including the following as abnormal bleeding: intermenstrual bleeding or spotting; postcoital bleeding; increased amount of bleeding at periods, or increased

^{*}Presented at a meeting of the Chicago Gynecological Society, April 15, 1955.

number of days of the menstrual period as compared to the patient's usual period; decrease of menstrual interval below 21 days; and postmenopausal bleeding. The latter was defined as bleeding one year or more after the cessation of menses. In each instance where abnormal bleeding was noted in the history, a diligent search was made for other generally accepted causes of abnormal uterine bleeding which seemed applicable in the particular case. In our studies, the residues of pelvic inflammatory disease are not listed as a cause of abnormal bleeding. Although many consider residues a cause we feel that this is an unproved point; in fact, in another study we are attempting to determine the precise cause-and-effect relationship of residues of pelvic inflammatory disease to uterine bleeding.

Regulte

In the 1,177 consecutive laparotomies on the Gynecological Service at the Chicago Wesley Memorial Hospital, endometriosis was diagnosed grossly 264 times: this is an incidence of 22.4 per cent in the patients subjected to laparotomy. The uterus was removed in 212. The tissue furnished microscopic confirmation of the gross diagnosis of endometriosis in only 119 of these 212 cases. Hence in 93 instances endometriosis could not be diagnosed in the available sections. The majority of these had been grossly described as "plaques" and "implants."

In the group where microscopic confirmation was possible, there were 40 cases of abnormal uterine bleeding, an uncorrected incidence of 33.7 per cent. The types of abnormal bleeding encountered are listed in Table I. Coexisting pathological conditions were found in 29 patients that could have caused the abnormal uterine bleeding. These are listed in Table II.

In the remaining 11 cases the abnormal bleeding did not seem to be satisfactorily explained by the coexisting pathology. Incidentally, 7 of these latter patients had secretory endometrium. It is also interesting that 6 of the 11 had incidental intramural or subserous fibroids, 2 had adenomyosis, and one had bilateral tuboovarian abscesses. None of these latter conditions is considered by us as an established cause of abnormal uterine bleeding. These 11 instances, in which the cause of bleeding seemed unexplained, represent a corrected incidence of unexplained abnormal uterine bleeding of 9.8 per cent of the 119 patients with a confirmed diagnosis of endometriosis subjected to hysterectomy.

TABLE I, TYPES OF ABNORMAL UTERINE BLEEDING IN PATIENTS WITH ENDOMETRIOSIS*

Intermenstrual bleeding	14
Postcoital spotting	2
Increased amount of bleeding at menses	32
Decreased interval to less than 21 days	3

The totals in this table add up to more than 40 because some patients had more than one type of abnormal bleeding.

TABLE II. ASSOCIATED PATHOLOGICAL CONDITIONS PROBABLY CAUSING ABNORMAL UTERINE BLEEDING IN ENDOMETRIOSIS SERIES

Submucous fibroids	11	
Endometrial polyps	9	
Carcinoma of the endometrium	1	
Acute cervicitis	1	
Endometrial hyperplasia	5	
Endocervical polyp	1	
Ectopic pregnancy	1	

Just as a matter of interest, we tabulated the incidence of abnormal uterine bleeding in the group of cases in which endometriosis had been diagnosed grossly but lacked microscopic confirmation. There were 93 such cases; 37 had some abnormality of uterine bleeding, a gross incidence of 38.8 per cent. In 11 of these cases also there was no intrauterine pathology to cause the bleeding, leaving a "corrected" percentage of 11.5 per cent.

For comparison, the group of patients who had not had a hysterectomy was also evaluated. The incidence of uncorrected abnormal uterine bleeding was only 12.5 per cent as compared to 33.6 and 38.8 per cent in the other two

groups.

There was a marked difference in the ages of the patients in the group without, as compared to the 2 groups with, hysterectomy. All of the group with "conservative" surgical procedures were under the age of 35, and 86 per cent were 30 or under. In the groups in which hysterectomies were done, the opposite was true, that is most patients were over the age of 30 and the majority were over 40. The age distribution in the 3 groups is shown in Table III. This age difference may have a bearing on the frequency of abnormal bleeding in any selected group since one would expect to find a higher incidence of uterine pathology in the older group. Undoubtedly in the older group more of the patients were operated upon for other conditions, and the endometriosis was merely an incidental finding.

TABLE III. AGE DISTRIBUTION

GROUPS	NO. IN GROUP	AGE IN YEARS			
		21-30	31-40	41-50	OVER 50
Uterus not removed	52	86.5%	13.5%	0	0
Uterus removed, gross diagnosis only	93	10%	37.7%	43%	8.6%
Uterus removed, microscopic confirmation	119	11.7%	39.4%	44.5%	4.4%

The sites of endometriosis seen at operation in the entire group are listed in Table IV. The ovary was affected most frequently, as one would expect.

TABLE IV. SITES OF ENDOMETRIOSIS

Ovary	117	
Uterosacral ligaments	39	
Rectosigmoid and cul-de-sac	41	
Broad ligament	22	
Bladder reflection	21	
Serosa of uterus	20	
Tube	9	
Round ligament	3	
Anterior abdominal wall	3	
Cervix	3	

In the entire series of 264 patients with gross evidence of endometriosis, 249 were white and 15 were Negro. There were 210 married women, 37.1 per cent of whom had never conceived.

Comment

The gross diagnosis of endometriosis seen in 22.4 per cent of the laparotomies done on our service varies sharply, as is to be expected, from the microscopically corrected incidence of 14.5 per cent. Most of the cases in which no confirmation was possible were of the group where the diagnosis of endometriosis

was incidental to other pathological findings and was based on the presence of small implants on the uterus, bladder, and the cul-de-sac. Nevertheless, it was quite interesting that the incidence of bleeding was practically the same in the confirmed group (with a higher incidence of larger lesions) and the unconfirmed group (with a higher incidence of small, scattered, unimportant lesions). It is also extremely interesting that in a younger age group (those in whom the uterus was not removed) the patients with endometriosis had a much lower gross incidence of abnormal uterine bleeding. These several observations suggest that endometriosis has little or nothing to do with abnormal uterine bleeding.

Apparently there is a good deal of variation as regards the incidence of endometriosis in various clinics across the country. In some areas it appears to be a rarity whereas here in the Midwest it is recognized grossly in more than one of five patients operated upon abdominally on a gynecological service. On the basis of microscopic confirmation it occurs in 14.5 per cent of all laparotomies.

Although 38 per cent of the patients involved complained of abnormal bleeding, on many occasions the only abnormality was a statement by the patient that her bleeding was "some heavier" or just "irregular for the past year or two." These cases were difficult to evaluate, and of necessity were included in the abnormal group. The findings in this series of patients certainly do not substantiate the popular concept that endometriosis is either a frequent or an important cause of abnormal uterine bleeding. It also follows that if one searches carefully a more likely local cause of abnormal uterine bleeding can usually be identified. Nevertheless, one must anticipate an unexplained increment since (a) the term "abnormal bleeding" is strictly a subjective symptom and (b) the exact mechanism of uterine bleeding remains such an enigma that every series of carefully analyzed cases of uterine bleeding must contain a certain percentage where "the exact cause has not been determined."

References

- Counseller, Virgil S., and Crenshaw, John L.: Am. J. Obst. & Gynec. 62: 930, 1951.
 Payne, F. L.: Am. J. Obst. & Gynec. 39: 373, 1946.
- Payne, F. L.: Am. J. Obst. & Gynec. 39: 373, 1946.
 Lamb, Woodbury, K.: California Med. 72: 113, 1950.
 Bookrajian, Edward N., and Morrow, Roy: J. M. Soc. New Jersey 47: 332, 1950.
 Dreyfuss, M. L.: Am. J. Obst. & Gynec. 39: 95, 1940.
 Kelly, F. J., and Schlademan, K. R.: Surg., Gynec. & Obst. 88: 230, 1949.
 Tyrone, C., and Weed, J. C.: South. M. J. 43: 107, 1950.
 Siegler, S. L., and Bisaccio, J. R.: Am. J. Obst. & Gynec. 61: 99, 1951.
 Preston, Stephen N., and Campbell, Harry B.: Obst. & Gynec. 2: 152, 1952.
 Te Linde, Richard W., and Scott, Roger B.: Am. Surgeon 17: 397, 1951.
 Randall, Clyde: J. A. M. A. 139: 972, 1949.
 Reschem, Clayton T.: J. A. M. A. 139: 971, 1949.

- 12. Beecham, Clayton T.: J. A. M. A. 139: 971, 1949.

Discussion

DR. FRED O. PRIEST .-- All of us have been guilty of accepting certain erroneous observations of our predecessors and statements made as facts in textbooks. Many of our ideas are changed when we carry out a study or examine our own experiences accurately. The observations made by Dr. Bayly and Dr. Gossack help to point out to us that certain symptoms commonly accepted as almost routine findings in a given pathological state may be grossly exaggerated.

In a review of the laparotomies over a similar length of time by the gynecologists of The Presbyterian Hospital, endometriosis was diagnosed grossly in 26 per cent of the cases. It was an incidental finding in many patients, the operation being done for other conditions. Although 40 per cent of these patients had abnormal bleeding from the records, coexisting pathology was present in a high percentage of the cases.

It is with the group treated conservatively, i.e., with the younger women in whom we make every effort to conserve the reproductive function, that such a study as this can be most accurately carried out. For it is in this group that we are less likely to find additional pathology which may be the etiological factor in abnormal bleeding. It should be pointed out that it may be very difficult to ascertain from the hospital record whether or not certain symptoms are present. One's own office record should be more dependable.

The essayists report an uncorrected incidence of 12.5 per cent of abnormal uterine bleeding in their group treated conservatively. In my own patients I have found abnormal bleeding in 20 per cent of these younger women. In some instances endometrial polyps were found, or adenomyosis was assumed because of the size and contour of the uterus. Both of these conditions, we believe, may disturb uterine bleeding. Even in this younger group, fibromyomas and disease of the cervix explained other cases of bleeding.

We agree with the authors that abnormal uterine bleeding does not occur with external endometriosis per se nearly so often as has been accepted as a fact. Although it is a coexisting symptom in a number of cases, we do not believe that the endometriosis is often etiological in the production of the abnormal bleeding. Until we are willing to accept one theory for the etiology of all endometriosis, we must at least consider the possibility that both the pathology and the symptom of abnormal bleeding may be due to the same etiological factor.

DR. EDITH L. POTTER.—Pelvic endometriosis is a diagnosis much more often made at the operating table than in the pathology laboratory. The small purplish areas observed by the surgeon often cannot be found in the specimen when it is examined in the laboratory and it is almost impossible to arrive at the total incidence of pelvic endometriosis from pathologic material.

Endometriosis involving the ovary, however, can be identified whenever it exists and I have selected the last 100 cases observed at the Chicago Lying-in Hospital for review. These have been seen during the past 8 years.

The median age of the patients was 37 years with the youngest 21 and the oldest 53. Forty-five per cent had never been pregnant and 23 per cent additional had had only 1 pregnancy.

The symptoms of which these patients complained showed great variability but some type of pelvic discomfort was encountered most often. This took the form of definite lower abdominal pain in 20, a bearing-down sensation in 6, and backache in 4. In 13 there was a statement of pelvic or abdominal mass with no definite record as to the main symptoms. In 23, or about half of these 43 patients, leiomyomas were present in the

There were 28 patients whose principal complaint was related to menstrual irregularities or bleeding. Ten complained of menorrhagia, 8 of menometrorrhagia, 10 of varying degrees of spotting or intermenstrual bleeding. Twenty of these 28 patients had some pathologic disturbance in the uterus that could well have been responsible for the bleeding. In 12 there were multiple leiomyomas, in 3 adenomyomas, and in 5 a diffuse hypertrophy of uterine musculature.

In 13 the principal complaint was dysmenorrhea. Three of these had accompanying leiomyomas; the other 10 had no uterine pathology.

Associated disturbances in the ovary were found in a total of 5; these included 2 small nonpapillary serous cysts, 2 small fibromas, and 1 dermoid cyst.

In the entire group of women with endometriosis of the ovary, 35 had accompanying leiomyomas, 3 had adenomyosis, 8 a diffuse hypertrophy of the myometrium, and 3 endometrial hyperplasia or a polyp.

In patients with some form of bleeding as one of the indications for operation there were only 8, or 8 per cent, who failed to have some other lesion that could have been the cause of the bleeding.

I agree with Dr. Bayly and Dr. Gossack that uterine bleeding is not a common symptom of "external endometriosis."

DR. EDWARD A. ALLEN.—Going back to the time that Sampson first described this condition and we began to operate upon it, we could not find endometriosis in anything like the proportion of patients in which he reported it. Tissue that we were sure had islands of endometriosis came back with a negative report. Shortly we acquired an anesthetist who also cut and stained our sections. She saw the gross lesion when it was removed and immediately our incidence began to climb rapidly because she went immediately to the laboratory, picked out the place that we were interested in that she had seen grossly, and made sections from it. At a later date due to the economies effected in laboratory work, we began to send our gynecological specimens to the general surgical laboratory. The incidence of endometriosis then dropped to almost nothing. For example, in a patient who had adenomyomas of the rectovaginal septum, or the rectum adherent to the fundus of the uterus by dense adhesions, the laboratory report would come back as corpus luteum cyst, etc. Then we began to use glass-headed pins to mark the distinctive lesions in the same manner as Dr. Brewer has just mentioned. Our incidence again began to climb. Our sections and our diagnoses tended more nearly to conform.

Another thing that I think is important in the diagnosis of endometriosis and its incidence is seen particularly in the cases of sterility. As you all know, these patients move from doctor to doctor, and sometimes are seen by as many as four or five in their attempts to get pregnant. Many of them obviously have never had a rectovaginal examination according to their own admissions or because they think I am examining them in the wrong place. I do not believe that the clinical diagnosis of endometriosis can be adequately made in many instances without rectovaginal examination and often without proper preparation of the patient by preceding enemas and preferably at the menstrual time when lesions are more tender and larger.

DR. BAYLY (Closing).—I have an idea that possibly we operate less frequently upon young patients with endometriosis than upon others, and it may be that there are quite a few devotees of stilbestrol therapy in our hospital.

If I am correct, Dr. Potter, most of your cases were limited to the ovary. We examined the pelvic structures looking for these plaques and did a resection wherever we saw them. Although we made an effort to put such tissue into solution and to get it to the general laboratory, we often failed to find the tissue later.

Dr. Greene has already mentioned our stromal requirements. In our fibroid cases, only submucous fibroids were blamed for abnormal bleeding. Intramural fibroids were present in most of our "unexplained" group, but we do not feel that such fibroids contribute to abnormal uterine bleeding.

I was glad that Dr. Allen pointed out too the differences in a general laboratory and a gynecological laboratory. At times things were pretty hot while we were working on this particular subject. We still feel that tissue was lost in the shuffle.

HODGKIN'S DISEASE AS IT AFFECTS THE PHYSIOLOGY AND ANATOMY OF THE FEMALE GENERATIVE TRACT*

JAMES P. HENNESSY, M.D., AND ANTONIO ROTTINO, M.D., NEW YORK, N. Y.

(From the Departments of Obstetrics-Gynecology, Medicine, and the Dorothy H. and Lewis Rosenstiel-St. Vincent's Hospital Hodgkin's Disease Research Laboratory)

In A previous communication we presented data pertaining to 52 cases of concurrent pregnancy and Hodgkin's disease. The disease became manifest during pregnancy in 21 of these patients, usually in the final months of gestation. In three, the diagnosis of Hodgkin's disease was established some time after parturition, and in 27 it antedated pregnancy. We failed to observe an increase in the tempo of the disease during pregnancy, nor did we note any unusual complications of the pregnancy or of the disease due to the concurrence of both states. Our conclusion was that pregnancy is not a hazard to the patient with Hodgkin's disease and that there is therefore no reason to interrupt pregnancy since adequate therapy can be administered to the mother (assuming of course that the proper safeguards are taken to protect the fetus against the effects of x-ray).

It is the purpose of the present report to supplement our first communication with data on menstruation and fertility. These data, obtained by questioning 31 patients currently being followed in the Hodgkin's disease clinic, are shown in Table I. We realize of course that our past and current cases are too few in number for satisfactory statistical study. However, they represent an experience over a period of ten years in an active, busy clinic.

Menstruation.—Of the 31 patients studied, 9 developed amenorrhea (Cases 2, 3, 10, 11, 14, 16, 17, 24, 27). Five of the patients (Nos. 11, 14, 16, 17, 27) had received x-ray therapy and amenorrhea began from a few months to a year following treatments. The remaining 4 (Nos. 2, 3, 10, 24) received no x-ray therapy but did receive nitrogen mustard, triethylene melamine (TEM) or both. In 6 cases the amenorrhea developed during a period of one and one-half to three years after the birth of their children. Five other patients. (Nos. 1, 4, 8, 13, 25) are experiencing oligomenorrhea, and 3 others have irregularity of the menstrual cycle. In none of these patients were these dysfunctions associated with clinically demonstrable diseases of tubes, ovaries, or uterus, but rather with the chronicity of the disease itself and with such manifestations of the disease as anemia and malnutrition.

Fertility.—Of the 21 married women forming part of our group, 10 have borne children, 5 have been unable to conceive, and 8 others who have desired additional children and are well within the physiologic childbearing age range have been unable to conceive and are classified as having secondary sterility.

That the presence of the disease per se does not cause sterility is attested by the fact that 4 patients (Nos. 7, 22, 23, 26) became pregnant after the disease had become established. One of these became pregnant ten months after

^{*}Presented at the Tri-City Meeting of the New York Obstetrical Society, April 12, 1955.

TABLE I. ANALYSIS OF MENSTRUATION AND FERTILITY IN 31 CASES OF HODGKIN'S DISEASE

CASE	CASE AGE STATUS NO. MONTHS 1. MW 23 Married 4½ years agnosed De 1951, in second month of p nancy. 36 m since onset		AGE STATUS NO. MONTHS SINCE ONSET			MENSTRUATION AFTER TIME OF ONSET OF HODGKIN'S DISEASE	FERTILITY. TIME AFTER ONSET OF HODGKIN'S DISEASE THAT PREGNANCY OCCURRED
1. MW			Hodgkin's disease diagnosed December, 1951, in second month of pregnancy. 36 months since onset of Hodgkin's disease	No change until De- cember, 1953, when it became scant and dark	Child born July 4, 1952, 7 months after onset of Hodgkin's dis- ease. No further pregnancies		
2. EF	29	Married 11 years	Hodgkin's disease diagnosed November, 1951. 30 months since onset of Hodgkin's disease	No change until af- ter birth of last child (third). Stopped suddenly 9 months after on- set of Hodgkin's disease	Two children before onset Hodg- kin's disease, and one 9 months after on- set of Hodgkin's disease		
3. MR	25	Married 7 years	Hodgkin's disease diagnosed 1946. Married 1947. Baby born 1948. 32 months since onset of Hodgkin's disease	Stopped suddenly 21 months after onset of Hodgkin's disease	Baby born Jan. 31, 1948, 13 months after on- set of Hodgkin's disease		
4. LG	41	Married 18 years	Hodgkin's disease diagnosed 1948, 72 months since onset of Hodgkin's disease	Gradual lessening. Stopped May, 1953. 61 months after onset of Hodgkin's disease. Not influenced by treatments	Two full-term children before Hodgkin's dis- ease. None since		
5. RC	31	Married 11 years	Hodgkin's disease diagnosed October, 1953. 5 months since onset of Hodgkin's disease	Gradual lessening. Amenorrhea. Last menstrual period February, 1954. 4 months after on- set of Hodgkin's disease	One child born 1945, before on- set of Hodgkin's disease. No fur- ther pregnancies		
6. AD	37	Single	Hodgkin's disease diagnosed June, 1953. Was seen 9 months after onset of Hodgkin's disease	No change. Last menstrual period December, 1953			
7. HR	29	Married 16 months		No change in menses. Last menstrual period Dec. 31, 1953. 10 months after onset of Hodgkin's disease			
8. MS	42	Married 25 years	Hodgkin's disease diagnosed in 1948. 72 months since onset of Hodgkin's disease	No change until 66 months after onset of Hodgkin's dis- ease. Began to lessen	Two full-term children before onset of Hodg- kin's disease		
9. TY	19	Single	Hodgkin's disease diagnosed in 1949. 60 months since onset of Hodgkin's disease	No change			

					FERTILITY. TIME AFTER ONSET OF
CASE	AGE	MARITAL STATUS	DURATION OF DISEASE. NO. MONTHS SINCE ONSET	MENSTRUATION AFTER TIME OF ONSET OF HODGKIN'S DISEASE	HODGKIN'S DISEASE THAT PREGNANCY OCCURRED
10. AC	25	Married 3½ years	Hodgkin's disease diagnosed February, 1954. 2 months since onset of Hodgkin's disease	Never any discom- fort. Has not menstruated since birth of last baby. Last menstrual period, April, 1953	First child born Dec. 17, 1951. Second child born Jan. 29, 1954, before on- set of Hodgkin's disease
11. JL	57	Married 33 years	Hodgkin's disease diagnosed March, 1948. 74 months since onset of Hodgkin's disease	Never any trouble. Last menstrual period, October, 1947. X-ray treat- ments	Two full-term children before onset of Hodg- kin's disease. None since
12. BS	45	Married 1½ years	Hodgkin's disease diagnosed 1952, 19 months since onset of Hodgkin's disease	No change. 19 months since onset of Hodgkin's dis- ease	Never pregnant
13. CS	18	Single	Hodgkin's disease diagnosed June, 1951. 35 months since onset of Hodgkin's disease	Scant for 3 months. Stopped May, 1953. 33 months since on- set of Hodgkin's disease	,
14. HY	27	Married 7 years	Hodgkin's disease diagnosed April, 1950. 54 months since onset of Hodgkin's disease	Always irregular. Dysmenorrhea. Last menstrual period, 1952. X-ray treatment for one year before it stopped. 28 months since onset of Hodgkin's disease	One child born Nov. 1, 1949, before onset of Hodgkin's dis- ease. No fur- ther pregnancie
15. MM	31	Married 7 years	Hodgkin's disease diagnosed 1948 after delivery of child. 70 months since onset of Hodgkin's disease	Always irregular. No change in 70 months since onset of Hodgkin's dis- ease	Child born March 1948. No fur- ther pregnancies
16. CW	28	Married 6 years	Hodgkin's disease diagnosed May, 1952. 33 months since onset of Hodgkin's disease	Always regular until she had x-ray treat- ments. Last men- strual period, May, 1952	
17. MM	34	Married 8 years	Hodgkin's disease diagnosed November, 1949, when she was 4 months pregnant with second child. Now 63 months since onset of Hodgkin's disease	Last menstrual period, October, 1951, following x- ray treatments	First child born July 24, 1947. Second child born May 3, 1950, 5 months after onset of Hodgkin's dis- ease
18. JP	31	Married 6 years	Hodgkin's disease diagnosed 1952. 36 months since onset of Hodgkin's disease	Always irregular and scant. No change since onset of Hodgkin's disease	Never pregnant

CASE AGE		SE AGE STATUS		DURATION OF DISEASE. NO. MONTHS SINCE ONSET	MENSTRUATION AFTER TIME OF ONSET OF HODGKIN'S DISEASE	FERTILITY. TIME AFTER ONSET OF HODGKIN'S DISEASE THAT PREGNANCY OCCURRED	
19.	ND	23	Single	Hodgkin's disease diagnosed May, 1950. Now 58 months since onset of Hodgkin's disease	Always irregular. No discomfort. Last menstrual period, January, 1955		
20.	RK	23	Single	Hodgkin's disease diagnosed January, 1953. Now 28 months since onset of Hodgkin's disease	No change		
21.	DP	23	Single	Hodgkin's disease diagnosed August, 1950. Now 57 months since on- set of Hodgkin's disease	No change		
22.	DR	23	Married 20 months	Hodgkin's disease diagnosed August, 1952. Now 20 months since onset of Hodgkin's dis- ease	No change	Onset August, 1952. Married Sept. 30, 1953. Preg. about 3 months, Decem- ber, 1953. De- livered July 1, 1954	
23.	BS	29	Married 2 years	Hodgkin's disease diagnosed February, 1950, two weeks after delivery of first child. 62 months since onset of Hodgkin's disease	Irregular until birth of baby. Regular ever since	One child born February, 1950. No further preg- nancies	
24.	sw	26	Married 6 years	Hodgkin's disease diagnosed January, 1953. 14 months since onset of Hodgkin's disease	Irregular, scant. Amenorrhea 11 months after onset of Hodgkin's dis- ease	Never pregnant	
25.	RF	31	Married 7 years	Hodgkin's disease diagnosed May, 1954. 10 months since onset of Hodgkin's disease		One child born Nov. 22, 1950, 42 months be- fore onset of Hodgkin's dis- ease. No fur- ther pregnancies	
26.	O'D	33	Married 2 years	Hodgkin's disease diagnosed March, 1954. 10 months since onset of Hodgkin's disease	No change. Last menstrual period, Jan. 15, 1955	Pregnant approx- imately 4 months, 9 months after on- set of Hodgkin's disease	
27.	SI	31	Married 3 years	Hodgkin's disease diagnosed March, 1949. 74 months since onset of Hodgkin's disease	Amenorrhea for 65 months following x-ray therapy	Never pregnant	

TABLE I-CONT'D

				FERTILITY, TIME AFTER ONSET OF HODGKIN'S DIS- EASE THAT PREG- NANCY OCCURRED	
28. TY	26	Single	Hodgkin's disease diagnosed January, 1955. 5 months since onset of Hodgkin's disease	No change	
29. ST	32	Married 8 years	Hodgkin's disease diagnosed January, 1952. 41 months since onset of Hodgkin's disease	No change	Two children, first in 1947, second in 1951. Both before onset of Hodgkin's dis- ease. No fur- ther pregnancies
30. AH	57	Married 25 years	Hodgkin's disease diagnosed March, 1955. 4 months since onset of Hodgkin's disease	No change. Last menstrual period, 1941	Never pregnant
31. SA	25	Single	Hodgkin's disease diagnosed March, 1955	No change	

the disease was diagnosed and was delivered of a normal child; the second, in whom the onset of disease occurred in August, 1952, and who married Sept. 30, 1953, delivered a healthy child July 15, 1954; the third patient is in the fourth month of pregnancy at the time of this writing, her disease having become manifest in 1950; and the fourth patient, with onset of disease in 1953, is now in the fourth month of pregnancy.

Symptoms Related to Pelvic Structures.—The only common symptom other than those related to menstruation is pain in the lower abdomen and back. A usual finding associated with this symptom is enlargement of pelvic nodes, these being detectable by palpation or vaginal examination. Relief of pain by x-ray therapy directed to pelvic nodes would support the opinion that the nodes in question are the cause of the back pain in some of these cases. Only once in our entire experience (Case 10) was Hodgkin's disease of the generative tract detected clinically and in this case the vagina was so affected that there was much edema of the vulva, the vaginal walls seemed hard and indurated, and narrowing of the entire vault was accompanied by a profuse yellowish discharge not unlike that in a malignancy. This patient died shortly afterward but there was no autopsy. Several patients in the course of the disease developed edema of the vulva. This was associated with enlargement of nodes in the groin and pelvis. It usually subsides with x-ray therapy to the nodes.

The rarity of involvement of the generative tract is confirmed by our autopsy experience. In the past nine years 39 autopsies have been performed on women dead of Hodgkin's disease, and in only 3 instances was there involvement (and this minimal) of the generative tract, as follows:

CASE 1.—(No. 3144.) There were miliary nodules of Hodgkin's disease over the pelvic peritoneum, including the uterus, but no evidence of the disease in the pelvic organs themselves (Fig. 1).



Fig. 1.—Case 1. Small, firm, gray nodules are implanted over the pelvic peritoneum and over a portion of the surface of the uterus. The substance of the ovary and uterus is not involved.

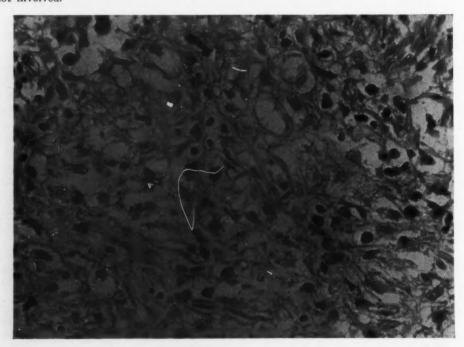


Fig. 2.—Case 2. Hodgkin's disease of the ovary. Reticulum cells and Sternberg-Reed cells. ($\times 750$; reduced $\frac{1}{4}$.)

Case 2.—(No. 3894.) There was microscopic involvement of both ovaries and tubes, the uterus being normal (Fig. 2).

CASE 3.—(No. 2218.) There was massive involvement of the pelvic cavity with infiltration of the urinary bladder. This patient had shown no striking clinical symptoms to direct attention to this organ. Uterus, tubes, and ovaries were not involved.

Summary and Conclusions

Data on 31 female patients with Hodgkin's disease who came under our observation are summarized in Table I and lead us to the following conclusions:

- 1. That Hodgkin's disease of the generative tract is a rare complication of the disease and that when it does occur it is minimal and of no functional significance.
- 2. That involvement of the pelvic nodes is not uncommon, the symptoms of such involvement being backache and edema of the vulva.
- 3. That the majority of patients afflicted with Hodgkin's disease show no evidence of it detectable by vaginal or rectal examination, but if followed for a period of years enlargement of the pelvic nodes may be detected by such examination.
- 4. That female patients with Hodgkin's disease may develop amenorrhea, oligomenorrhea and sterility.

Reference

1. Hennessy, J. P., and Rottino, A.: AM. J. OBST. & GYNEC. 63: 756, 1952.

PATHOGENESIS OF POLYCYSTIC OVARIES*+

SHELDON C. SOMMERS, M.D., AND PERCY J. WADMAN, M.D., BOSTON, MASS.

(From the Departments of Pathology and Gynecology, Massachusetts Memorial Hospitals and the Departments of Pathology, Boston University School of Medicine and Harvard Medical School)

FOR many years multiple follicular cysts of both ovaries have been observed, but Stein and Leventhal were among the first to correlate such polycystic ovaries with clinically evident disease. The accompanying triad of (1) menstrual irregularity particularly with amenorrhea, (2) sterility, and in half the cases (3) hirsutism comprises the Stein-Leventhal syndrome. By "polycystic" is meant the presence of multiple usually closely adjacent follicular cysts with granulosa-cell linings.

A pathologic examination that was undertaken in the present study of ovaries from 740 unselected female autopsied cases permitted the collection of 26 instances of bilateral polycystic change (3.5 per cent). The incidence in this selected population composed largely of older women probably has little bearing on the frequency in living patients, such as might attend a gynecologic clinic. It was reported from Finland² that a polycystic ovary was observed in 7.19 per cent of 12,160 cases operated upon, and in 1.4 per cent the change was bilateral.

When the series of 26 cases was completed, other pertinent clinical and pathologic material was assembled to determine what additional abnormalities there were, and to attempt to elucidate the origin of the ovarian cysts and related changes. Pituitary cell counts were made using the periodic acid-Schiff stain and method of Rasmussen.³ Studies of similar conditions in women and animals in the literature were also reviewed.

Review of Literature

Polycystic ovaries have been reported in the newborn of diabetic mothers⁴ and in children with precocious puberty.⁵ In adult women with acromegaly,^{6,7} or less specific pituitary hyperfunctional states with mixed or alleged chromophobe adenomas,^{8,9} the same ovarian lesions have been found. Also, in 36 of 73 collected premenopausal instances of endometrial carcinoma,¹⁰⁻¹⁵ and some young patients with breast cancer,¹⁶ the ovaries were polycystic.

The Stein-Leventhal syndrome, as judged by recent reports, 17-21 has as its central pathologic feature bilateral polycystic ovaries. Clinically 80 to 100 per cent of affected women had menstrual disturbances, 35 to 100 per cent were sterile, 43 to 68 per cent were hirsute, 10 to 38 per cent obese, and 0 to 38 per

^{*}This investigation was supported by research grants C1754 (R) and C2480 from the National Cancer Institute, of the National Institutes of Health, U.S. Public Health Service.

†Presented in part at a meeting of the New England Surgical Society, Boston, April 13, 1955.

9

0

e

d

f

r

e

r

cent had acne. The syndrome may occur during pregnancy.²² Breasts were described as under-¹ or overdeveloped,¹⁹ and the clitoris as unchanged¹⁹ or enlarged.²¹ Those avoiding eponyms usually have termed the condition ovarian masculinization.^{22, 23} Several authors have considered the ovarian changes to be due to disorders or excesses of gonadotropic hormone secretion.^{4, 12, 19, 23}

Experimentally, numerous reports indicate that adult women treated with gonadotropins of pituitary, chorionic, or pregnant-mare-serum origin develop typical polycystic ovaries, without ovulation.²³⁻²⁵ Sheep pituitary gonadotropin containing chiefly follicle-stimulating hormone (FSH) has been widely used in inducing a striking ovarian enlargement and the formation of multiple follicular cysts.²⁵

It has been known for over thirty years that in rats injections of pituitary extract would produce enlarged unruptured ovarian follicles.26 Unilateral oophorectomy or ovarian traumatization in rats²⁷ and rabbits²⁸ led to follicular cyst formation, ascribed to induced stimulation by pituitary gonadotropins. Ovarian homeotransplants²⁹ into rats' eyes developed enlarged follicles in both spayed females and intact males, known to secrete chiefly a FSH type of gonadotropin. Pituitary extracts containing gonadotropins produced similar effects after injection into guinea pigs.30 In animals given growth hormone injections³¹ or bearing transplanted pituitary tumors secreting thyroid-stimulating hormone the same ovarian reaction observed has been ascribed to the otherwise disturbed pituitary functions of the host.32 Experimental parabiosis with unilateral castration led to the development of polycystic ovaries in the intact female partner.33,34 This has been ascribed to the preponderance of gonadotropins in a preparation with two active pituitary glands and only one set of ovaries.³⁵ Hypothalamic damage to dogs³⁶ and rats³⁷ caused the development of polycystic ovaries, indicating a center controlling pituitary activity in this part of the brain.

A considerable variety of clinical and experimental evidence thus uniformly favors pituitary gonadotropic stimuli of FSH type as the cause of polycystic ovary formation both in man and in various animal species.

Present Series

Among the 26 cases collected for analysis, there were two children, $2\frac{1}{2}$ and 9 years old at death, 23 women of childbearing age, and one 75 years old, presumed to have had polycystic ovaries for 30 or more years.

Both the children had brain abnormalities. The younger died of meningitis after a suboccipital craniotomy and laminectomy in an attempt to correct hydrocephalus and Arnold-Chiari malformation. Spina bifida and myelomeningocele were also present. The older was a diabetic child with multiple cerebral gliomatous nodules at autopsy. Two young women, 16 and 23 years old, had brain tumors. The former had diplopia, nystagmus, internal hydrocephalus, and died after operation for a fibrillary astrocytoma thought to have arisen in the pons. The latter also had diplopia, neurofibromatosis, and died after removal of a left cerebellopontine neurofibroma. Other intracranial lesions of neurofibromatosis were found at autopsy. In these 4 female patients with central nervous system disease there was evidence of pressure and damage in the optic chiasmal region, with damage likewise to the hypothalamus.

The 21 other adult premenopausal women were 16, 17, 19, 21, 25, 26, 26, 30, 32, 33, 34, 34, 35, 35, 35, 37, 37, 47, 47, and 47 years old. Excluding the patient 75 years old and the children the average age was 31 years. Ten women were married and 4 had had children; 6 were ostensibly sterile. There were menstrual data provided for only 7 women, and all were abnormal. Four women had had irregular menses since the menarche, for a total of 3 to 12 years. Two had had scanty flow, and in 2 the periods had been regular but scanty. Three women had had amenorrhea for 2 to 6 month intervals.

Among the 21 adult women with adequate records 8 were obese by standard height-weight tables, 4 had diabetes mellitus, 2 had abnormal hirsutism and 1 had acne.

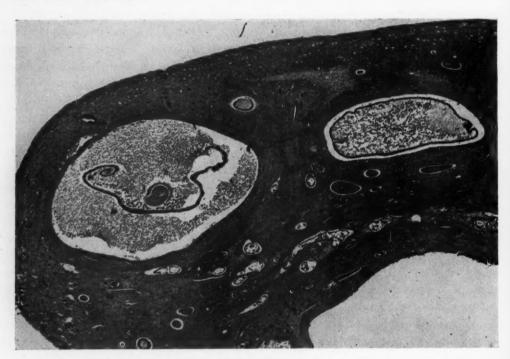


Fig. 1.—Polycystic ovary from a child $2\frac{1}{2}$ years old, who had abundant cervical epithelial glycogen and endometrial hyperplasia. (Hematoxylin and eosin. $\times 10$; reduced $\frac{1}{10}$.)

The major diseases causing death included pulmonary tuberculosis in 6 women, none with genital involvement. Four had cancer, including an incidental basal-cell carcinoma of lip in the oldest patient. There were 3 fatal cases of cancer, 2 women each 34 years old died of breast tumors, and 1 patient 37 years old of carcinoma of the stomach. Cardiac disease was the cause of death in 4 women, 2 cases rheumatic and 2 hypertensive in type. One in each cardiac group also had active glomerulonephritis.

Clinically manifest endocrine diseases diagnosed included 4 instances of diabetes mellitus, 3 in adults 19, 26, and 47 years old. The 2 younger women died of sepsis, and the oldest of diabetic nephropathy. One patient 35 years old died after a thyroidectomy performed for thyrotoxicosis, and 2 others had pathologic primary thyroid hyperplasias. One 37-year-old woman had alcoholic cirrhosis.

The 5 remaining women died of sepsis or infections, including one case of postoperative peritonitis after colectomy for Hirschsprung's disease, one after

lobectomy for bronchiectasis, and a third after ileostomy for nonspecific ulcerative colitis. There was also one fatal brain abscess and one case of bulbar poliomyelitis at autopsy.

All the available organs were reviewed microscopically and gross pathologic findings were also scrutinized. Except for the endocrine glands and their target organs no significant abnormalities were found, aside from the lesions of the major diseases already mentioned.

Ovaries.—All 26 cases showed numbers of follicular cysts, from 3 to 12 per microscopic section, lined by granulosa cells in one to three layers. (Figs. 1 and 2). In 2 cases there were foci of granulosa-cell hyperplasia. The cysts pressed against each other and were oriented in a line beneath the surface.

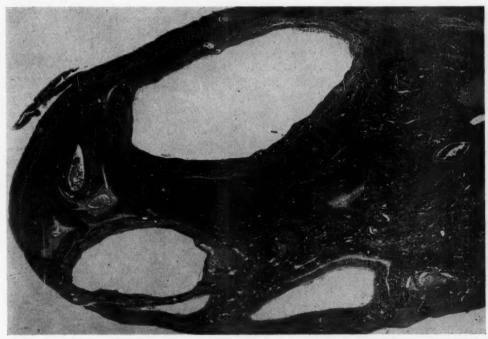


Fig. 2.—Multiple follicular cysts of ovary, from a patient 35 years old, who died of tuberculosis. Endometrial hyperplasia, cystic mastitis, and nodular goiter were found. (Hematoxylin and eosin. $\times 10$; reduced $\frac{1}{16}$.)

The ovarian stroma superficial to the cysts was uniformly thickened and the primordial ovallay at a deeper stratum than normally (Figs. 3 and 4). The ovarian stromal hyperplasia was composed of the usual closely packed spindle cells with intercellular empty spaces indicative of abundant lipoid content, and occasional whorled nodules between the cysts. Grossly the ovarian surfaces were pearl gray, smooth, and shining, like the tunica vaginalis testis. The stroma beneath was yellow tan and the responsible lipids were partly alcohol soluble in such fixative. Ova were not observed in the great majority of the follicular cysts, because of either their degeneration or planes of section. Corpora lutea were present in 4 of 23 adult patients. Theca lutein cysts and medullary vascular hyperplasia were each present in ovaries of one patient.

In a case of granulosa-cell carcinoma in a woman 36 years old, not included in this series, it was of interest that the contralateral ovary was polycystic and had cortical stroma hyperplasia.³⁸



Fig. 3.—Thickened superficial ovarian stroma, with primordial ova shown as light dots, and polycystic change, from a tuberculous woman 32 years old. (Hematoxylin and eosin. $\times 13$; reduced $\frac{1}{16}$.)

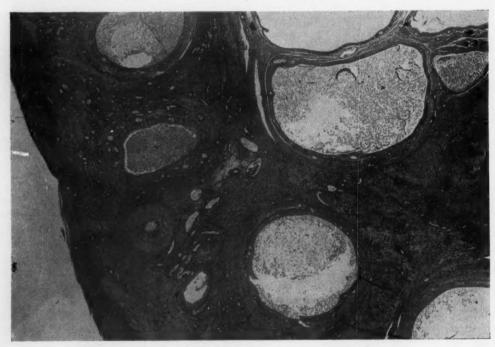


Fig. 4.—Hyperplastic ovarian cortical stroma overlying multiple follicular cysts. The patient, aged 25 years, died of pollomyelitis. Menses had been irregular since childbirth 1 year previously. (Hematoxylin and eosin. $\times 15$; reduced %.)

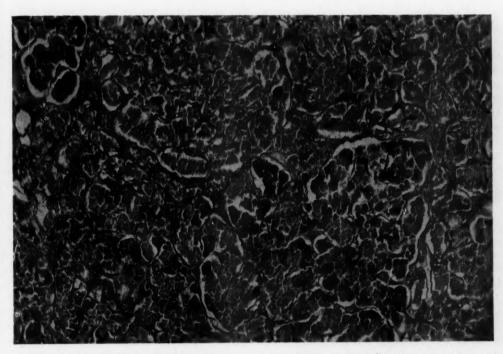


Fig. 5.—Pituitary basophil hyperplasia, shown as nodules of dark cells, from the same child as Fig. 1. (Pearse periodic acid-Schiff stain. $\times 150$; reduced $\frac{1}{16}$.)



Fig. 6.—Nodular basophil hyperplasia of anterior pituitary, from a 19-year-old girl with polycystic ovaries, endometrial hyperplasia, and mammary adenofibrosis. Death was ascribed to diabetic coma. (Pearse stain. $\times 150$; reduced $\frac{1}{16}$.)

Endometrium.—Hyperplasia of cystic or adenomatous type was found in 12 of 24 cases, including 2 with endometrial polyps. The 2½-year-old child had endometrial hyperplasia and estrogen effect of adult type in the cervical epithelium. There was one normal adult secretory endometrium, the other 10 were inactive.

Breast.—In 14 of 15 cases with available specimens there were abnormalities, including 8 with adenofibrosis and 6 with chronic cystic mastitis. Two of the latter group also had mammary carcinoma simplex. Most of the cysts ob-

served were of the blunt duct type.

Thyroid.—Among 25 glands examined, 9 were abnormal (36 per cent). Lesions included 3 cases of primary hyperplasia, 2 of atrophy, 2 with an abnormally nodular architecture, one nodular goiter, and one diffusely hypertrophied gland weighing 55 grams in a woman of 34 years with breast cancer, hirsutism, acne, and large but not hyperplastic adrenals.

Thymus.—Two women, aged 16 and 35 years, had large persistent glands. Pituitary.—All 7 glands available showed on routine examination unusual numbers of normal heavily granulated basophils collected into hyperplastic nodules (Figs. 5 and 6). Cell counts after the method of Rasmussen confirmed increased proportions of basophils in each case. The average of 31.4 per cent basophils was nearly twice that for a control group of premenopausal women, 16.3 per cent. Since two children were included in the polycystic ovary group, the contrast to normal is actually more marked, since prepubertal girls have fewer basophils (Table I). Other cell types were not significantly altered, except for a striking reduction in amphophils. These cells are thought to produce thyrotropic hormone (TSH), and possibly other factors.³⁹

TABLE I. PITUITARY CELL COUNTS WITH PERIODIC ACID-SCHIFF STAIN (Every fifth field in every fifth row counted to a maximum of 10,000 cells)

AGE	DISEASE	NO. OF CELLS	ACI- DOPHIL	BASO- PHIL	AMPHO- PHIL	CHROMO- PHOBE	HYPER- TROPHIC AMPHOPHIL	HYALINE BASOPHII
Polyc	ystic Ovaries, 7 cases.—							
21	Hydrocephalus	3,622	32.8%	27.5%	1.2%	38.3%	0.3%	0%
9	Diabetes	3,826	30.0	29.4	2.9	36.0	2.0	0.1
16	Astrocytoma	5,378	37.3	32.9	6.1	21.2	2.4	0.1
19	Diabetes	8,573	38.8	29.9	2.3	27.5	1.3	0.4
21	Brain abscess	7,788	51.9	30.0	1.7	16.3	0.3	0
25	Poliomyelitis	10,418	25.9	43.0	5.5	23.6	1.8	0.1
35	Glomerulonephritis	10,109	46.2	26.5	2.3	23.6	1.6	0
Ave	rage	7,102	37.5%	31.4%	3.1%	26.5%	1.4%	0.1%
Contr	ols, 10 cases.—							
23	Poliomyelitis	7,746	42.7%	14.4%	16.5%	24.5%	1.2%	0%
24	Poliomyelitis	5,033	46.8	19.9	9.6	22.9	0.6	0
29	Uremia	9,895	41.7	20.0	22.0	15.4	0.8	0.1
29	Disseminated lupus	11,367	47.1	17.1	14.6	19.1	1.1	0
31	Poliomyelitis	10,522	58.5	12.2	12.8	15.6	0.9	< 0.1
32	Brain abscess	10,615	51.8	16.2	12.2	19.3	0.4	< 0.1
39	Cerebral hemorrhage	4,189	30.9	18.2	21.5	28.4	0.9	0
42	Cerebral aneurysm	9,507	43.2	16.5	11.6	28.0	0.6	0.1
42	Cerebral thrombosis	6,770	43.3	14.1	19.2	21.4	0.9	0
43	Meningitis	6,733	56.6	14.0	10.4	18.1	0.9	0
Aver	rage	8,238	46.3%	16.3%	15.0%	21.3%	0.8%	< 0.1

Pancreas.—The islets of Langerhans were increased in size and number in 2 women, one 37 years old with stomach carcinoma, and one 47 years old with tuberculosis. In the diabetic women the islets appeared reduced in size and number. Other cases were negative.

Adrenals.—The zona reticularis was prominent in 4 women but not definitely hyperplastic, as is seen in the adrenogenital syndrome. The zona fasciculata was nodular in 3 cases.

Comment

Reconstruction of patients' various pathologic lesions and clinical findings has been attempted in this study, starting with the presence of bilateral polycystic ovaries. No case with multiple bilateral follicular cysts was excluded, although the autopsy population from which the series was obtained is recognized as a selected group.

Viewed together these women were a rather homogeneous group pathologically. Pituitary basophilism, polycystic ovaries, and mammary fibrocystic disease were usually present together. Endometrial hyperplasia occurred in half the cases, and the remainder of the uteri were inactive, perhaps due to the effects of the major disease present. Reproduction had been successful in only 4 of 10 women, suggesting that the group was relatively sterile. Some women apparently acquired polycystic ovaries some time in the middle of the reproductive age period. The average age of 31 years was corroborative of this. It was of interest to find instances in childhood and in old age.

The normal pituitary basophils present in significantly increased numbers are of the type considered from animal and human data, including histochemical evidence, to secrete the gonadotropic hormone of FSH type.^{39, 40} Inferred excessive FSH secretion is thus concluded as being responsible pathogenetically for the polycystic ovarian changes, without excluding the likely controlling role of hypothalamic dysfunction, particularly implicated in the 4 cases with brain lesions. Interpreted most simply, these patients had a form of endogenous Aschheim-Zondek or Friedman test reaction to their own excessive gonadotropins.

It is emphasized that ovarian growth as well as cyst formation had occurred, with a uniform hyperplasia of the cortical ovarian stroma. The superficial thickening of hyperplastic stroma indeed likely provided a mechanical barrier and made ovulation difficult or impossible, with consequent sterility. Premenopausal women or children who possessed primordial ova developed polycystic ovaries upon excessive gonadotropic stimulation, while postmenopausal women lacking ova capable of maturation have been found to form solid nodular masses of hyperplastic ovarian stroma without follicular cysts. ⁴¹ Put in other words, polycystic ovaries are in younger women analogous to cortical stromal hyperplasia in women beyond the reproductive period. Gonadotropic overstimulation of FSH type can occur at any age. From birth to middle age FSH hyperstimulation led to development of polycystic ovaries; thereafter to cortical stromal hyperplasia. Either form of ovarian response has apparently been morphologically irreversible, although the abnormal pituitary stimulation theoretically may be transient.

Target organs of ovarian estrogen in this series were found to be most responsive and most uniformly affected. Breast and endometrium gave evidence of a prolonged stimulation leading to proliferation and cystic or ade-

nomatous epithelial hyperplasia. From other reports it appears that endometrial and breast carcinomas^{11-13, 16} are the most frequent neoplasms accompanying polycystic ovaries. Evidence at hand has emphasized the significance of continued estrogen stimulation in the background of these two types of cancer, particularly as a prerequisite priming agent.^{16, 34, 42}

Pituitary-adrenal dysfunctions supervening during the evolution of malignant transformations in endometrium and breast are considered elsewhere. 16, 42

Thyroid control by pituitary TSH has been known to have some relationship, as yet poorly understood, to gonadotropic functions.³² The incidence of 36 per cent thyroid abnormalities in this series is corroborative. Unfortunately, none of the cases with thyroid lesions had pituitary glands available for examination, and no information about FSH-TSH interrelations could be assembled. The pituitary amphophils considered to produce TSH were found to be reduced in numbers. Significant adrenal and pancreatic islet abnormalities were not observed, and, if the clinical observations of obesity, hirsutism, and diabetes mellitus were attributable to abnormalities of these endocrine glands, they have occurred chiefly at a functional level. Based on animal experiments, the two instances of hyperplasia of the pancreatic islets are attributable to estrogen.⁴³

The Stein-Leventhal syndrome, as previously defined,¹ could not be applied to the entire group of women studied, since 40 per cent were parous and only 10 per cent hirsute. Admittedly, clinical information was incomplete. It is desirable, however, to stress that not all cases of bilateral polycystic ovaries are recognizable by history and physical examination alone, and probably half such cases would be overlooked on clinical examination. Recognition of women with polycystic ovaries is important for at least two reasons: (1) sterility due to anovulation is curable in many cases by surgical therapy; (2) significant precancerous endometrial or breast changes resulting from the uninterrupted secretion of ovarian estrogen can be alleviated surgically by puncturing or otherwise breaking the cysts, and thereby interrupting a vicious cycle in which thickened ovarian cortices are one factor.

Summary

Pathologic observations and clinical correlations are analyzed in the cases of 24 women and 2 children found at autopsy to have bilateral polycystic ovaries. Pituitary basophilism with an inferred FSH hypersecretion, likely under hypothalamic control, was considered responsible for the observed ovarian stromal hyperplasia and the formation of multiple follicular cysts. Breast, endometrium, and occasionally pancreatic islets responded to the uninterrupted ovarian estrogenic stimulation. Clinical stigmas of the Stein-Leventhal syndrome were evident in only about half of the women with polycystic ovaries.

Appreciation is expressed to Drs. A. T. Hertig and G. K. Mallory for advice in the preparation of the manuscript.

References

- 1. Stein, I. F.: Am. J. Obst. & Gynec. 50: 385, 1945.
- Vara, P., and Niemineva, K.: Acta obst. & gynec. scandinav. 31: 94, 1951.
 Rasmussen, A. T.: Am. J. Path. 9: 459, 1933.
 Hamilton, G. M.: J. Obst. & Gynaec. Brit. Emp. 60: 533, 1953.

- 5. Pray, L. G.: Pediatrics 8: 684, 1951.
 6. Cushing, H., and Davidoff, L. M.: Rockefeller Inst. Med. Research, N. Y., 1927, Monograph No. 22.
- 9. Werner, P.: Am. J. Med. 16: 363, 1954.

 10. Jones, H. O., and Brewer, J. I.: AM. J. OBST. & GYNEC. 42: 207, 1941.

- 11. Speert, H.: Surg., Gynec. & Obst. 88: 332, 1949.
 12. Sommers, S. C., Hertig, A. T., and Bengloff, H.: Cancer 2: 957, 1949.
 13. Dockerty, M. B., Lovelady, S., and Foust, G. T., Jr.: Am. J. Obst. & Gynec. 61: 966, 1951
- Orrahood, M. D., and Wyatt, J. P.: J. Obst. & Gynaec. Brit. Emp. 60: 859, 1953.
 DeVere, R. D., and Dempster, K. R.: J. Obst. & Gynaec. Brit. Emp. 60: 865, 1953.
 Sommers, S. C.: Lab. Invest. 4: 160, 1955.

- Sommers, S. C.: Lab. Invest. 4: 160, 1955.
 Frank, I. L.: M. Clin. North America 32: 1611, 1948.
 Ingersoll, F. M., and McDermott, W. V., Jr.: Am. J. Obst. & Gynec. 60: 117, 1950.
 Greenblatt, R. B.: Postgrad. Med. 9: 492, 1951.
 Andrews, M. C.: Virginia M. Monthly 79: 544, 1952.
 Buxton, C. L., and Van de Wiele, R.: New England J. Med. 251: 293, 1954.
 Alexander, W. S., and Beresford, O. D.: J. Obst. & Gynace. Brit. Emp. 60: 252, 1953.
 Geist, S. H., and Gaines, J. A.: Am. J. Obst. & Gynec. 43: 975, 1942.
 Geist, S. H., Gaines, J. A., and Salmon, U. J.: Am. J. Obst. & Gynec. 42: 619, 1941.
 Davis, M. E., and Hellbaum, A. A.: J. Clin. Endocrinol. 4: 400, 1944.
 Evans, H. M.: Harvey Lectures, Philadelphia, 1923-1924, 19: 212.
 Wang, G. H., and Guttmacher, A. F.: Am. J. Physiol. 82: 335, 1927.
 Emery, F. E.: Physiol. Zool. 4: 101, 1931.
 Goodman, L.: Anat. Rec. 59: 223, 1934.

- 29. Goodman, L.: Anat. Rec. 59: 223, 1934.
- Goodman, L.: Anat. Rec. 59: 223, 1934.
 Morrin, K. C., and Loeb, L.: Proc. Soc. Exper. Biol. & Med. 32: 1425, 1935.
 Moon, H. D., Simpson, M. E., Li, C. H., and Evans, H. M.: Cancer Res. 10: 549, 1950.
 Furth, J.: Am. J. Path. 30: 421, 1954.
 Bielschowsky, F.: Brit. J. Cancer 8: 154, 1954.
 Sommers, S. C., and Chute, R. N.: A. M. A. Arch. Path. 61: No. 3, 1956.
 Bielschowsky, F., and Hall, W. H.: Brit. J. Cancer 5: 331, 1951.
 Heinbecker, P.: Medicine 23: 225, 1944.
 Hillarp, N. A.: Acta endocrinol. 2: 11, 1949.
 Sommers, S. C. Gates, O. and Good of L. L.: Obst. & Gynes, 6: 395, 1955.

- 38. Sommers, S. C., Gates, O., and Goodof, I. I.: Obst. & Gynec. 6: 395, 1955. 39. Purves, H. D., and Griesbach, W. E.: Endocrinology 49: 244, 1951.
- 40. Friedgood, H. B.: Endocrine Function of the Hypophysis, New York, 1946, Oxford University Press.
- Woll, E., Hertig, A. T., Smith, G. V. S., and Johnson, L. C.: AM. J. OBST. & GYNEC. 56: 617, 1948.
 Meissner, W. A., and Sommers, S. C.: Am. J. Path. 31: 571, 1955.
 Foglia, V. G., Penhos, J. C., and Cardeza, A. F.: Compt. rend. Soc. biol. 148: 1656, 1954.

THE PSP (PHENOLSULFONPHTHALEIN) TEST FOR TUBAL PATENCY*

GEORGE SPECK, M.D., AND PAUL E. HALTER, M.D., ARLINGTON, VA.

THE phenolsulfonphthalein test was created as a tool to determine the patency of the Fallopian tubes—an important factor in the study of infertility. Several articles have been written over the past several years since the introduction of the test in 1948, some favorable 1-6, 11, 12 and others unfavorable.7-10

We have considered the criticisms which will be the subject of a future paper, and have reviewed our own results. We appreciate the pitfalls of subjective scrutiny, yet honestly believe that our conclusions today are as valid as they were in 1948.

We have refined the technique of the test and have substituted quantitative analyses of our results for qualitative in evaluating patency of the tubes.

Technique

The vagina and cervix are prepared in the same manner as for an insufflation test or hysterosalpingography. All instruments are surgically sterile. The bladder is emptied. A Graves' speculum is inserted into the vagina. The cervix is grasped with a tenaculum. Without preliminary probing of the cervical canal (as suggested in the original report) a cannula (Rubin or Kahn) with a rubber obturator at the tip is inserted into the cervical canal. The rubber obturator should be no more than $\frac{1}{2}$ to 1 inch from the tip so that when it fits snugly against the external os the tip reaches almost to the internal os and no regurgitation of phenolsulfonphthalein can occur. It is better not to go beyond the internal os, for traumatization of the endometrium may occur with resulting absorption of the dye, interfering with the accuracy of the test. A screw type of cannula should never be used. Ten cubic centimeters of phenolsulforphthalein† (each cubic centimeter containing 0.6 mg. of phenolsulforphthalein) is drawn up in a 10 c.c. syringe. (The same solution can be made by diluting one ampule containing 6 mg, phenolsulforphthalein with 10 c.c. of sterile water or normal saline.) The needle is removed from the syringe, and the syringe is then inserted into the open end of the cannula. The phenolsulforphthalein solution is injected slowly. At 4 to 5 c.c., when the uterine cavity is filled, some resistance is met. If the tubes are open, this resistance is quickly overcome and another few cubic centimeters of the solution are easily injected. By slow injection of a few cubic centimeters at a time, intermittent resistance is overcome with little distress to the patient. Cramping is felt which quickly disappears when the 10 c.c. is completely injected. If the tubes are closed or there is diminution in the size of the lumen, resistance to the flow of phenolsulforphthalein increases after about 5 c.c. is injected. Some of the dye will regurgitate about the rubber obturator and be visible in the vagina, and the patient will complain of severe pain. When this occurs, it is best to

^{*}Presented at a meeting of the Washington Gynecological Society, March 26, 1955. †Special ampules were prepared by Hynson, Westcott & Dunning, Inc., of Baltimore, Md.

pause for about a minute and then try to inject more phenolsulfonphthalein. If the resistance is due to temporary spasm, more phenolsulfonphthalein can be injected; if the tubes are closed, the resistance and pain will be maintained and it is advisable not to inject additional dye. When all the phenolsulfonphthalein has been injected, or all that can be injected, the stopcock at the distal end of the cannula is closed to prevent any reflux of the solution.

The cannula is removed at the end of 10 minutes. A tampon is placed in the vagina and the speculum and tenaculum are removed. The patient is not given any water to drink. At the end of an additional 20 minutes the bladder is catheterized and all of the urine is collected in a clean graduate. To the urine is added 10 per cent sodium hydroxide solution by drops until no further color change is noted. If the volume of the urine is less than 100 c.c., distilled water is added until a volume of 100 c.c. is reached; if over 100 c.c., enough water is added to make 200 c.c. (In the latter case the quantitative reading is multiplied by 2.) If the urine shows a concentration of more than 10 per cent phenolsulfonphthalein, the tubes are considered to be adequately patent; if between 5 and 10 per cent there is diminution in the caliber of the lumen; if negative or under 5 per cent, the tubes are either closed or damaged severely enough to constitute a negative test as far as fertility is concerned.

Results

The phenolsulfonphthalein test was performed 121 times. The first 64 tests were done qualitatively and the last 57 tests quantitatively. When the Rubin test was performed, it was done immediately before the phenolsulfonphthalein test. Hysterosalpingograms were done either within a few days following the phenolsulfonphthalein test or at the mid-period of the following cycle.

A. Qualitative Tests.—

In 46 cases the tubes were known to be patent. The phenolsulfonphthalein test was correctly positive in all but 2 cases; in 38 Rubin tests, correctly positive in all but 3 cases; and in 6 hysterosalpingograms, in all but 1 case. In analyzing the errors it was found that in 2 cases both the phenolsulfonphthalein and Rubin tests showed nonpatency of the tubes, whereas hysterosalpingography showed the tubes to be patent. In one case, however, the uterus was bicornate with patency in one tube only; and in the other case, when operation was performed, both tubes were bound down by dense adhesions.

In 6 cases the tubes were known to be closed and in all cases the phenolsulforphthalein test was correct. The Rubin test and hysterosalpingography were done in 1 case each and were correct.

In 12 cases of tubal ligation, the phenolsulfonphthalein test showed non-patency of the tubes correctly in 6 cases and showed them possibly incorrectly patent in 2. We say "possibly" because these 2 tests were done on the same patient following religation. After bilateral ligation was done by the Pomeroy technique the phenolsulfonphthalein test showed tubal patency which was substantiated at operation. After religation the phenolsulfonphthalein test was persistently positive whereas the Rubin test showed nonpatency. In 4 cases the phenolsulfonphthalein test was positive for tubal patency, which was substantiated by hysterosalpingography.

B. Quantitative Tests .-

In 57 cases, quantitative determinations of the phenolsulfonphthalein test were done.

In those patients in whom the tubes were known to be patent, the phenolsulfonphthalein test was done with the Rubin test 27 times, and with hysterosalpingograms as well as Rubin tests 7 times. Out of 27 cases of known tubal patency, the phenolsulfonphthalein test was definitely positive in 23. In 6 cases, the results of the phenolsulfonphthalein tests were in disagreement with those of the Rubin tests. In 3 cases, the phenolsulfonphthalein test was in error; in 3, the Rubin test; and in 1 both were incorrect.

A breakdown of the errors, however, disclosed that although the tubes were patent according to hysterosalpingography functionally they were probably impervious to a fertilized ovum. In these cases where the phenolsulfon-phthalein test was less than 5 per cent but the Rubin test revealed patency, hysterosalpingography showed patency in 1 tube only. We feel, however, that though there was patency the normal physiology of the tube was probably distorted for in 1 case an acute exacerbation of chronic salpingitis occurred 3 days after hysterosalpingography with resulting pyosalpinx and hydrosalpinx. In another there was delayed filling of the tube and in the third a previous salpingectomy had been performed.

In 3 cases, the phenolsulforphthalein tests were positive for patency, but the Rubin tests showed nonpatency of the tubes. In all 3 cases hysterosal-pingography revealed the tubes to be patent.

In the 1 case where both phenolsulfonphthalein and Rubin tests showed nonpatency of the tubes, hysterosalpingography showed 1 tube to be patent but with a defect at the cornu and the opposite tube distorted with moderate delay in filling.

Thus, in our hands, the Rubin and the phenolsulfonphthalein tests were equal in their accuracy when performed on patients with known patency of the tubes.

In 10 cases of known nonpatency of the tubes, the phenolsulfonphthalein test was correct in all but 1 case. The Rubin test was correct in all 10.

In 20 cases of tubal ligations, 2 ligations were done by us and 18 by Dr. Elmer Macht, Jr., at Bellevue Hospital, New York, N. Y. It is in this group that the greatest error was found, with 5 definitely positive results, or 25 per cent false positives. It is in this area (tubal ligation) that the greatest source of error has occurred with other investigators. We do not believe that this invalidates the test but suggests that in tubal ligations there may be specific factors contributing to "false positive" results. These may be: incompletely tight closures, allowing leakage of phenolsulfonphthalein; inversion of the serosal surface after healing, permitting absorption to take place at the distal end of the tube; and variations in the technique of ligations. We are not convinced that there is enough absorption from normal endosalpinx, as suggested by Hofmann, to give a positive test, for then it would be expected in all tubal ligations—which certainly was not true in our hands or in the hands of others. The suggested is all tubal of the suggested to the suggested of the suggested in the lands of others.

Since it is apparent, however, that a source of error may be present when phenolsulfonphthalein tests are done following tubal ligation, it is suggested that other tests be substituted in these cases.

Summary

In 73 cases of known tubal patency, the phenolsulfonphthalein test was positive in 67 cases, giving an accuracy of 91.8 per cent. Done by the same investigators, and on the same patients, 65 Rubin tests were correct in 58 cases, an accuracy of 89.2 per cent.

In 16 cases of known nonpatency, the phenolsulfonphthalein test was incorrect in 1 case—93.75 per cent. In the 11 cases in which the Rubin test was also done, all were correct—100 per cent accuracy.

In cases of known tubal ligation, the phenolsulfonphthalein test was performed 32 times. In 7 cases, the test was falsely positive and in 4 cases correctly positive as proved by hysterosalpingogram. In the use of the phenolsulforphthalein test following tubal ligation is the only deviation from the high standard of accuracy that has been encountered.

We still feel that the phenolsulforphthalein test is simple, physiologic, safe, and accurate. We feel that it will show gross patency and nonpatency of the tubes as accurately as the Rubin test.

When the return of phenolsulforphthalein in the urine is 10 per cent or better, the tubes may be considered patent to the passage of an ovum. When the return is less than 10 per cent, one or both tubes are either closed or sufficiently altered to prevent the passage of an ovum. In these latter cases, hysterosalpingography is advised to determine the degree and area of tubal nonpatency or reduced patency.

Furthermore, we strongly suggest that in performance of the test the technique as outlined be carefully followed and no substitutions made, especially in the type of cannula and amount of phenolsulfonphthalein used.

References

- Speck, G.: Am. J. Obst. & Gynec. 55: 1048, 1948.
 Palán, F.: Časop. lék. česk. 88: 388, 1949.

- 3. Gori, R. M.: Obst. y ginec. latino-am. 7: 606, 1949. 4. Speck, G.: J. A. M. A. 143: 357, 1950. 5. Israel, S. L., and Freed, C. R.: Fertil. & Steril. 1: 328, 1950.
- 6. Brown, W. E.: Discussion of Israel and Freed.5
- 7. First, A. E.: Discussion of Israel and Freed.5
- 8. Rosset, E. M.: Am. J. OBST. & GYNEC. 60: 892, 1950.
- 9. Hofmann, T. R.: AM. J. OBST. & GYNEC. 61: 1154, 1951.
 10. Hofmann, T. R.: Personal communication, August, 1951.
 11. Davis, M. E., Ward, M. E., and King, A. G.: Fertil. & Steril. 3: 217, 1952.
- 12. Hamm, O. L.: Personal communication, October, 1952.

2808 SOUTH RANDOLPH STREET

PHYSIOLOGIC ENDOSALPINGITIS?

H. A. SMITH, M.D., AND R. R. GREENE, M.D., CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology, Northwestern University Medical School and Wesley Memorial Hospital)

THE term "physiological salpingitis" has recently been proposed by Nassberg, McKay, and Hertig¹ for a mild degree of endosalpingitis found during menstruation and supposedly due to irritation of the endosalpinx by a reflux of menstrual blood and debris. It was noted that 62.3 per cent of uterine tubes removed from 69 menstruating patients showed some degree of inflammation. The findings indicating inflammation were considered to be edema of the tubal plicae, stasis of leukocytes within the capillaries, dilation of lymphatics, presence of polymorphonuclear leukocytes in the lumen of the tube, and presence of polymorphonuclear leukocytes in the stroma of the plicae. In addition, the presence of red blood cells, "hemoglobin debris," and of endometrial debris in the tubal lumen was noted. The data also were analyzed for the frequency of these various changes in early menses, midmenses, and late menses. The findings were most impressive in the midmenstrual period.

The concept of "physiological salpingitis" was new to us and was received with sympathy by at least one of the present authors. In a few preliminary observations of tubes associated with menstrual endometrium, minimal inflammatory changes in the endosalpinx did seem to be present. A systematic study of this phenomenon was therefore undertaken. It was believed necessary, however, to include similar tabulations on tubes associated with nonmenstrual endometrium. In the original article by Nassberg, McKay, and Hertig, no detailed data were given on the findings in control tubes. The authors did state, however, "In a control group of several hundred cases, this inflammatory reaction was not found in the tubes associated with proliferative or secretory endometrium of the remaining 23 days of the endometrial cycle."

Materials and Methods

Originally our series contained (a) 100 uteri with menstrual endometrium and with one or both tubes, and (b) a control group of 100 uteri with proliferative or secretory endometrium and one or both tubes. In these groups were included specimens with old healed follicular salpingitis but without dilatation of the tube. It was believed that since there was no dilatation of the tube the communication between the tube and the uterus was probably patent. After tabulation of all of the data, however, it was discovered that 12 specimens with follicular salpingitis were included in the menstruation group and only 3 with this particular diagnosis were present in the control group. This added a bias to our data since there was no actual proof that the tubal uterine communication was patent in these patients. The 12 specimens with

follicular salpingitis in the menstrual group were, therefore, discarded as were the three specimens from the control group. To even up the series, the last 9 in the normal control group were also discarded. This left a group of 88 cases in the menstrual group and 88 in the nonmenstrual control group. In many instances in each group an occasional isolated lymphocyte or plasma cell was found in the stroma of the tubal plicae. If a diligent search is made such cells are apparently commonly found in this location. With the exception of these findings (which we consider to be normal) there was no evidence of "chronic" inflammation in these tubes.

The materials were obtained from the files of our departmental laboratory and include specimens from women from 23 to 50 with an approximately even age distribution in the two groups.

Observations

The endometrium was graded as to day of menses on the basis of the microscopic findings. For the most part these agreed with the clinical history. With some of the very early menses the patients were not bleeding clinically and in some of the older cases the clinical histories do not include data regarding menstrual bleeding. Other phases of the cycle were also determined by the microscopic findings. In most instances these agreed with the clinical history.

Detailed tabulations were made of: (1) edema of tubal plicae, (2) dilation of plical lymphatics, (3) pooling in and lining of vessel walls with polymorphonuclear leukocytes—leukostasis, (4) extravascular polymorphonuclear leukocytes in the stroma of the tubal plicae, (5) polymorphonuclear leukocytes in the tubal lumen, (6) presumably endometrial cells and their debris in the tubal lumen, and (7) red blood cells in the tubal lumen. These are the findings tabulated by Nassberg and his associates.

Findings

The detailed tabulations are shown in Table I. It should be noted that the figures in this table represent the presence or absence and not the degree of a particular finding. With the exception of dilation of the lymph vessels in the plicae, the various findings were more common in the tubes of menstruating women than in those of nonmenstruating women. The differences were not very great and in only one instance (edema of the tubal plicae) was the difference between the two groups significant (by the chi square method).

TABLE I. COMPARISON OF THE FINDINGS IN MENSTRUAL AND NONMENSTRUAL TUBES

	MENSTRUAL	NONMENSTRUAL
Total number	88	88
Edema of plicae	27	15
Dilation of lymphatics	56	57
Leukostasis	44	41
Polymorphonuclear leukocytes in lumen	17	12
Polymorphonuclear leukocytes in stroma	26	17
Cellular debris in lumen	26	18
Red cells in lumen	30	26

As previously stated the data in Table I indicate the presence or absence of the various findings and not the degree or magnitude of the involvement. Accordingly those tubes from the two groups showing either endometrial debris in the lumen or polymorphonuclear leukocytes in the stroma were restudied. The findings were tabulated as to "slight, moderate, and marked."

There was no great difference in the amount of endometrial debris in the two groups; e.g., of the menstrual group, 7 had a moderate and 19 had a slight amount; whereas in the control group 1 was marked, 3 moderate, and 14 slight. On the other hand, there was a fairly definite difference in regard to polymorphonuclear leukocytes in the stroma. In the control group only one specimen showed a moderate number of polymorphonuclear leukocytes in the stroma. In 16 others only a "slight" number were present. In the menstrual group, of 26 that had polymorphonuclear leukocytes in the stroma, 7 had a moderate number and 2 were tabulated as "marked."

It is not known exactly how long a menstrual endosalpingeal inflammatory reaction, if present, would persist. It was, therefore, considered possible that the tubes of some of the early proliferative group might still have residual changes caused by a reflux of menstrual blood.

Table II compares the findings in tubes associated with proliferative endometrium with those associated with secretory endometrium. Except for dilation of plical lymphatics and the presence of red blood cells in the tubal lumen, the findings were more common in the proliferative than in the secretory group. The difference was rather marked in cases of leukostasis, polymorphonuclear leukocytes in the stroma, and polymorphonuclear leukocytes in the tubal lumen. Only in this last instance, however, was the difference statistically significant.

TABLE II. COMPARISON OF THE FINDINGS IN PROLIFERATIVE AND SECRETORY PHASES

	PROLIFERATIVE	SECRETORY
Total number	44	44
Edema of plicae	9	6
Dilation of lymphatics	26	31
Leukostasis	25	16
Polymorphonuclear leukocytes in lumen	10	2
Polymorphonuclear leukocytes in stroma	11	6
Cellular debris in lumen	10	8
Red cells in lumen	13	13

Table III compares the findings in the menstrual group with those of the secretory group only. Since there were a different number of cases in the two groups, the comparisons are made on the basis of percentages. Excluding "dilation of plical lymphatics," the findings were greater in each instance in the menstrual than in the secretory groups. These differences were statistically significant in so far as edema of the tubal plicae and the presence of polymorphonuclear leukocytes in the stroma as well as in the tubal lumen were concerned. These three findings are certainly indicative of an inflammatory reaction. It therefore seems evident that an endosalpingeal inflammatory reaction is found more commonly during menses than during the secretory stage of the cycle.

TABLE III. COMPARISON OF FINDINGS IN MENSTRUAL WITH SECRETORY PHASE

	MENSTRUAL	SECRETORY
Total number	88	44
Edema of plicae	30.1%	13.6%
Dilation of lymphatics	63.6%	70.4%
Leukostasis	50.0%	36.3%
Polymorphonuclear leukocytes in lumen	19.3%	4.5%
Polymorphonuclear leukocytes in stroma	29.9%	13.6%
Cellular debris in lumen	29.9%	18.1%
Red cells in lumen	34.1%	29.5%

For the sake of completeness, the findings in early, mid-, and late menses were compared (Table IV). These data perhaps show a trend toward the various findings being more common in early menses, less so in midmenses, and least so during late menses. We do not understand why this should be so, nor the significance of this finding.

TABLE IV. COMPARISON OF THE FINDINGS IN THE DIFFERENT STAGES OF MENSES

	EARLY MENSES	MIDMENSES	LATE MENSES
Total number	29	32	27
Edema of plicae	12	8	7
Dilation of lymphatics	19	21	16
Leukostasis	20	10	14
Polymorphonuclear leukocytes in lumen	10	6	1
Polymorphonuclear leukocytes in stroma	. 14	7	5
Cellular debris in lumen	14	9	3
Red cells in lumen	15	12	3

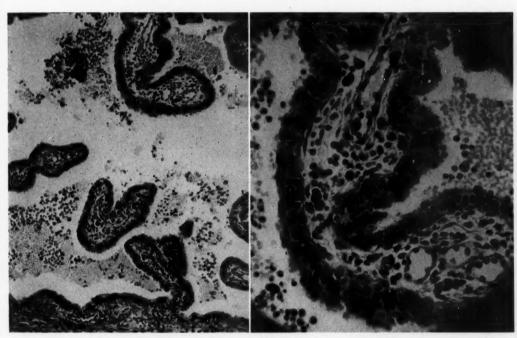


Fig. 1

Fig. 2.

Fig. 1.—NUMS. Gyne. No. 8344.) Low power of tube removed during menses. Cells, cellular debris, and blood are present in the lumen. (×120; reduced ¼.)

Fig. 2.—(NUMS. Gyne. No. 8344.) High power of Fig. 1. Polymorphonuclear leukocytes are present in the stroma of a plica. (×360; reduced ¼.)

Comment

The fairly frequent presence of a small amount of cellular debris and occasional red blood cells in the lumina of otherwise normal tubes has long been noted in our laboratory. We had considered it to be a phenomenon produced by trauma. All specimens from the gynecologic services of Passavant Memorial Hospital and Chicago Wesley Memorial Hospital are submitted to this laboratory after the hospital pathologists have cut their blocks. In both of these institutions, after the patient is anesthetized, she is examined by the

resident, the intern, and frequently the clerk. One of us at least (R. R. G.) has thought that this repeated squeezing of the uterus could well force materials from the endometrial cavity into the tubal lumina. On the other hand, this is merely a "thought" for which there is no valid evidence. We have not compared these findings with those in tubes from patients who were not subjected to multiple examinations under anesthesia just prior to operation. Also, we have no evidence that all of these cellular elements are necessarily of endometrial origin.

In general, our findings confirm those of Nassberg, McKay, and Hertig. The phenomenon of physiologic salpingitis probably does occur occasionally and probably is due to a reflux of menstrual blood and debris. Our findings disagree with theirs in that evidences of an inflammatory reaction were less common in our menstrual series. Perhaps the Middle Westerner is a less sensitive creature! Our findings also differ in that evidences of inflammation

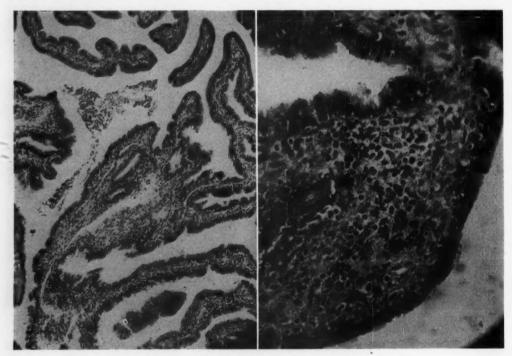


Fig. 3.

Fig. 4.

Fig. 3.—(NUMS. Gyne, No. 18015.) Low power of tube removed during proliferative phase of menstrual cycle. Cellular debris and red blood cells are present in the lumen. (×100; reduced 1/4.)

Fig. 4.—(NUMS. Gyne. No. 18015.) High power of another area from same slide used in Fig. 3. Polymorphonuclear leukocytes are present in the stroma of a plica. (×400; reduced ¼.)

were found in some of the tubes from nonmenstrual patients. These tended to be more common in the proliferative than in the secretory stage. It is possible that some of the inflammatory changes found in the proliferative phase were a residue of a more active inflammatory reaction in the antecedent menstrual phase.

Finally, it should be stated that in our series in only one menstrual case did the degree of inflammatory reaction ever approach that pictured by Nassberg and co-workers. If the tubes illustrated in their article are an average, then we cannot agree as to the degree of inflammation. Fig. 1 is a photograph showing the most marked change in our series.

Summary and Conclusions

Detailed tabulations and analyses have been made of the various findings indicating a possible acute inflammatory reaction in the otherwise normal endosalpinges of 88 women who were menstruating and 88 who were not. Such an inflammatory reaction was found in a moderate number of tubes from the menstrual group. A similar reaction was found in a lesser number of tubes from the nonmenstruating control group. A statistically significant difference could not be shown between the menstrual and the control groups, although the degree of infiltration of the stroma by polymorphonuclear leukocytes was greater in some of the tubes in the menstrual group than was apparent in the control group.

When a comparison of the findings in menstrual patients was made with those in patients in the secretory phase, significant differences were found. This latter comparison was made because it seemed possible that some of the tubes of the proliferative phase might still have a residuum of a possible acute inflammatory reaction persistent from the previous menstrual phase.

It was concluded that an acute inflammatory reaction in the endosalpinx may occasionally be caused by or at least be associated with menstruation and that the term "physiologic endosalpingitis" is applicable.

Reference

 Nassberg, Seymour, McKay, Donald G., and Hertig, Arthur T.: Am. J. Obst. & Gynec. 67: 130, 1954.

Department of Case Reports New Instruments, Etc.

CHORIONEPITHELIOMA FOLLOWING FULL-TERM PREGNANCY* Case Report

A. E. KANTER, M.D., AND ROBERT BAUER, M.D., CHICAGO, ILL.

E. N., a 34-year-old Negro woman, gravida vii, para vi, was admitted to Cook County ton. Hospital on Aug. 26, 1954, complaining of vaginal bleeding of thirty-four days' duration. Her past obstetrical history included an ectopic pregnancy in 1951 and six normal spontaneous deliveries, the last of which was on June 3, 1954, at home. Then the patient had a 7 pound female infant and delivery was recorded as uneventful, with the placenta complete and no excessive bleeding. The patient stated she was well until July 23, at which time vaginal bleeding started which had persisted until the day of admission. The week prior to admission she had passed clots the size of an egg. She denied sexual relations up to a few days before admission. A review of symptoms showed a cough for ten days, hemoptysis for five days, and a weight loss of several pounds in the past few weeks.



Fig. 1.—Chest plate with classic metastatic lesions.

Physical examination showed a well-developed Negro woman in no apparent distress. The temperature was normal, pulse 88, and respirations 20. There were a few moist râles at the lung base. The cervix was transversely lacerated and softened. The corpus was enlarged to the size of a 10 to 12 weeks' gestation. There was a slight mucosanguineous discharge. The impression was subinvolution of the uterus with retained secundines—rule out hydatid mole. An Aschheim-Zondek test was ordered and dilatation and curettage scheduled.

^{*}Presented at a meeting of the Chicago Gynecological Society, Jan. 21, 1955.

On August 29 a curettage was performed which revealed a large amount of hyperplastic endometrium. There was no excessive bleeding. On September 1, the Aschheim-Zondek test was reported as positive. The pathological report from the curettage was secretory endometrium with decidual reaction. No placental tissue was seen on the specimen submitted. A chest plate showed pulmonary metastases of the "snowball" type

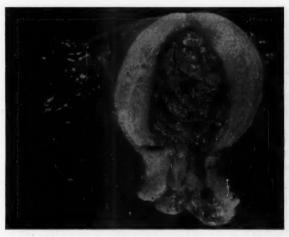


Fig. 2.—Gross specimen showing fungating chorionepithelioma filling cavity of uterus.

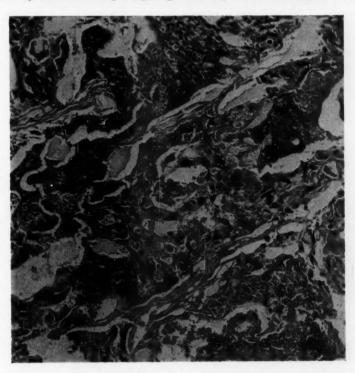


Fig. 3.-Microscopic section of tumor.

(Fig. 1). On September 3, a total abdominal hysterectomy and right salpingo-oophorectomy were performed (the left tube and ovary being absent from the previous operation). No abdominal or vaginal metastases were noted. The cavity of the uterus contained a polypoid tumor mass (Fig. 2). The microscopic sections were reported as follows: "There are

large areas of hemorrhage and necrosis surrounding obvious large islands of extremely malignant-appearing tumor cells. There is much pleomorphism. There appear to be both Langhans and syncytial cell types. Diagnosis, chorionepithelioma of the uterus with invasion' (Fig. 3).

Postoperatively, the patient received blood and broad-spectrum antibiotics, but continued to have fever ranging from 99 to 102° F. daily, as well as bloody sputum and dyspnea. On September 9, she felt better and was afebrile. A chest plate showed new metastases. Her appetite was improving. Low-grade fever persisted thereafter.

On the tenth postoperative day, in consultation with the Departments of Radiation Therapy and Hematology and because of their previous poor results with radiation therapy in this disease, treatment was instituted with nitrogen mustard as a possible palliative measure. A dose of 4 mg. per kilogram of body weight or a total of 24 mg. was given intravenously in four divided doses on consecutive days. Atropine and intravenous fluids were also given to alleviate nausea and vomiting during the course of treatment. On September 18, the sixteenth postoperative day, the nitrogen mustard therapy was completed. Marked subjective improvement was noted for approximately two weeks but x-ray findings continued to grow worse, fever persisted, and dyspnea returned, and on October 23 (fifty-two days after operation, ninety-two days after the onset of symptoms, and 142 days after delivery) the patient died. Permission for autopsy was refused.

Conclusions

A case of chorionepithelioma has been presented, typical in its history, except that it followed a full-term pregnancy which is less common than following hydatid moles, striking in its rapidly fatal clinical course. Treatment with operation and nitrogen mustard did not alter the course of this disease.

NORMAL PREGNANCY AFTER RECOVERY FROM METASTATIC CHORIOCARCINOMA

WILLIAM B. PATTERSON, M.D., PUUNENE, MAUI, HAWAII

(From Puunene Hospital)

T WAS my fortune to have referred to me a patient at the fourth month of I gestation who had been operated upon three years and seven months previously for a tumor of the spinal column which had proved to be a choriocarcinoma. A similar case could not be recalled and after search nothing could be found that would help me in caring for this patient. This, of course, is what one would expect because hysterectomy has been the accepted treatment, with which the author has concurred, for choriocarcinoma as well as for repeated positive pregnancy hormone tests following hydatidiform mole. This patient continued through pregnancy normally except for premature labor at about 35 weeks' gestation. At the present time, five years and four months after removal of choriocarcinoma from the spine and seventeen months after delivery, she has a normal-appearing child, is apparently well herself, and one year ago returned to her usual work. This case was thought to be worthy of reporting in detail, not so much because it might help others in treating similar rare cases, but because it might throw some light on the etiology of this most malignant tumor.

Case Report

Mrs. D. T., aged 26 years, gravida ii, para 0, was referred to me on Aug. 20, 1952, by Dr. G. S. Haywood of Puunene, Maui. She gave the following relevant history:

Menses began at the age of 12, regular every 30 days and painless. The flow was

normal in amount and lasted six to seven days.

On July 5, 1947, she had been examined by Dr. W. T. Dunn of Lahaina, Maui, because of amenorrhea since April 27 and had been found to be pregnant. Complete blood count, urinalysis, blood Wassermann test and blood pressure were normal. On July 29, she was normal except for mild edema of the ankles. She was next seen on August 12 and had gained 6 pounds in two weeks. She had developed moderate anemia with a red blood cell count of only 3.12 million per cubic millimeter. The urine contained 4 plus albumin and granular casts. The blood pressure had risen from 105/70 to 160/90. In five weeks' time the uterus had enlarged from the size of a two months' pregnancy to that of a five months' pregnancy. She was admitted to the Lahaina Hospital for observation. A diagnosis of hydatidiform mole with toxemia was made and dilatation and curettage were performed on August 23. A large amount of grapelike tissue was removed and the patient made a good recovery, being discharged on August 28. The tissue was not sent to a pathologist for study.

She was seen at follow-up examinations every two weeks and made a normal recovery. On Oct. 9, 1947, six and one-half weeks after evacuation of the mole, a Friedman hormone test was positive though there had been no abnormal vaginal bleeding. Because of this a dilatation and curettage of the uterus were done but very little tissue was obtained and it was not examined pathologically. The uterus was normal in size.

On Dec. 6, 1947, a Friedman hormone test was again positive but clinically the patient was well and nothing was done.

A Friedman hormone test was strongly positive on Jan. 28, 1948. At this time she had had a chocolate-colored vaginal discharge for ten days followed by five days of apparently normal menstruation. Pelvic examination showed the uterus to be of normal size. A blood count was normal. A dilatation and curettage of the uterus were done on February 10 and again very little tissue was obtained and it was not sent for pathological examination.

Normal menstruation occurred on March 25 and recurred normally thereafter. In October, 1948, she developed a rectal abscess which was treated surgically with recovery.

On April 5, 1949, a Friedman hormone test was negative.

A curettage was done by Dr. W. T. Toney of Lahaina, Maui, on June 13, 1949, because of excessive menstruation for sixteen days which could not be controlled with the usual medications. The uterus was normal in size and only a small amount of tissue was obtained. This tissue was sent to Dr. I. L. Tilden, pathologist of Honolulu, T. H., who

reported, "Diagnoses: endometrium, showing follicular activity; degenerated material."

Normal menstruation occurred after this last curettage and she had a normal period on Sept. 19, 1949. On October 17 she developed pain in the right thigh which persisted in spite of frequent treatments. She did not menstruate in October but on November 12 began to have a scanty flow which lasted for three days. She developed tenderness over the left sacroiliac joint as well as dysuria. Because of the persistent pain in the thigh and back and because of the history of having had a hydatidiform mole she was referred on Nov. 11, 1949, to Dr. H. E. Bowles, obstetrician and gynecologist of Honolulu, T. H., for study and diagnosis.

Dr. Bowles reported pelvic examination to be normal except for cervical erosion. Cytological smears from the cervical canal and from the cervical erosion were negative for malignancy. The cervix was cauterized with hot cautery and the patient was then referred to Dr. John J. Lowrey, neurosurgeon of Honolulu, T. H., for an opinion as to the cause of the pain in the back and thigh.

Dr. Lowrey found many sensory and motor changes in the lower extremities. X-ray showed a narrowing of the lumbosacral interspace without other abnormalities. He thought she probably had a herniated intervertebral disc with pressure on the fifth lumbar and first sacral nerve roots. He prescribed bed rest for two weeks and medication for pain. Then she was to be fitted with a back support and was gradually to resume activity.

After two months of this treatment there was a progression of the neurological findings so on Jan. 15, 1950, she was admitted to the Queen's Hospital, Honolulu, T. H., for a myelogram (Hospital No. 25534). This showed a defect between the fourth and fifth lumbar vertebrae and a complete block at the fifth lumbar and first sacral interspace suggesting a large herniated disc or tumor. The spinal fluid showed no cells and a total protein of 80 mg. per 100 c.c.

On Jan. 19, 1950, Dr. Lowrey did a laminectomy and removed an intraspinal tumor. The following is taken from the note on his surgical procedure: "... it was apparent that there was extreme intraspinal pressure and what appeared to be tumor material exuded out of the small hole where the ligamentum flavum was removed. A laminectomy of L-5 and S-1 segments was done and a large mass of tumor tissue which was soft and fragmented easily was removed from about the L-4, 5, S-1 and S-2 roots. This tumor extended anteriorly clear around the cord and also on the left side. The dura appeared to be involved but I was not sure of this and did not open the dura."

Friedman hormone tests were done on Jan. 27 and 31, 1950, but both were atypical. The rabbit's ovaries were enlarged and contained many nonhemorrhagic follicles. An x-ray of the chest on Jan. 27, 1950, was normal. The patient made a prompt recovery from the operation without any progression of the neurological signs.

Pathological examination of the tumor tissue removed from the spine was done by Dr. Sumner Price of Honolulu, T. H. He reported that the findings were typical of

choriocarcinoma. The diagnosis was choriocarcinoma. The tissue was also examined by Dr. I. L. Tilden, who concurred in the diagnosis. (On Feb. 27, 1952, slides from the tumor were presented to the Hawaii Society of Pathologists and all members thought that choriocarcinoma was the correct diagnosis. On March 1, 1955, a slide from this tumor was examined by Dr. Emil Novak, chairman of the committee on the Mathieu Memorial Chorionepithelioma Registry, and he, personally, agreed with the diagnosis of choriocarcinoma.) In Fig. 1 masses of relatively small cells are present with vesicular nuclei corresponding to the Langhans cells of choriocarcinoma and in the middle irregular giant

Fig. 1.

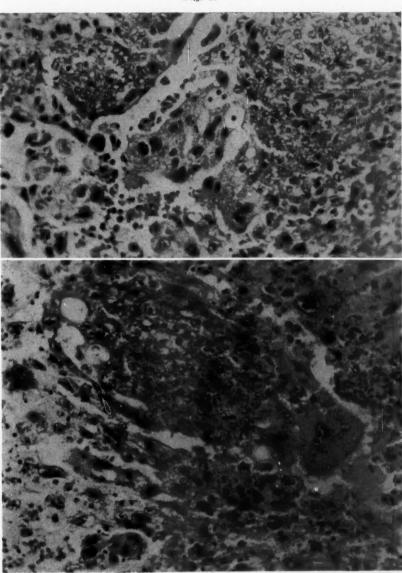


Fig. 1.—Masses of small cells with vesicular nuclei are present representing Langhans cells, and syncytial giant cells with dark nuclei are present at the periphery. (Hematoxylin and eosin. ×265.)

Fig. 2.—A mass of relatively small cells of Langhans type is present in the middle and larger, darker cells and one giant cell are present at the periphery and on the right side. (Hematoxylin and eosin. ×265.)

cells are present with multiple nuclei which stain very deeply. Many of these were present and they were thought to represent syncytial cells. In Fig. 2 similar changes are noted. There is one large giant cell with multiple nuclei on the right-hand side of the photograph.

X-ray treatments were begun on Jan. 30, 1950, and continued daily through Feb. 11 by Dr. L. L. Buzaid, radiologist at the Queen's Hospital. One portal was used, posterior lumbosacral, and 200 r was given daily for a total of 2,400 r.

The patient was discharged from the hospital on Feb. 20, 1950, ambulatory with a back support. Her neurological signs had disappeared except for absent ankle jerks. She was followed by Dr. Lowrey at six-month intervals. X-rays of the back were normal on Feb. 21, 1951. On Feb. 20, 1953, she was well except for a diminished right ankle jerk.

After returning home following operation and x-ray therapy she developed cystitis and then diarrhea which required much treatment throughout the year. X-ray of the chest was normal in December, 1950.

She had had a normal menstrual period in January, 1950, before operation on the spinal column but did not menstruate after x-ray treatment until March, 1951, when normal menses recurred. A pelvic examination done in April, 1951, was normal and the uterus was small.

During the next year she was relatively healthy. She was treated several times for minor complaints, once after a coconut fell on her head. She had returned to work as a personnel clerk in a busy pineapple cannery.

In August, 1952, she had a diagnosis of hyperthyroidism because of symptoms of weight loss, fatigue, excessive perspiration, exophthalmos, and enlargement of the thyroid gland. She received treatment for this and improved, though it is not known what medication she was given.

In April, 1953, she consulted Dr. G. S. Haywood who diagnosed thyrotoxicosis because of marked exophthalmos, loss of 25 pounds of weight in one year, a rapid pulse, a basal metabolic rate of plus 34 per cent and an enlarged thyroid gland. X-ray of the chest at this time was normal. She was given propyl thiouracil for one month and the basal metabolic rate fell to minus 3 per cent. After consultation with Dr. Lowrey and others it was felt that she should have a subtotal thyroidectomy which was done by Dr. Haywood on June 5, 1953, at the Puunene Hospital (Hospital No. K11494). She made a good recovery from the operation and was discharged on June 13. The histologic examination showed "diffuse hyperplasia of the thyroid."

At pelvic examination on June 1, 1953, before thyroidectomy Dr. Haywood noted that the uterus was the "size of an average multiparous uterus" but that it was softer than normal. The patient had had a normal menstrual period about the middle of April but she had only two days' flow in May. She returned to work on July 1 after thyroidectomy but was asked to return for a pelvic examination in August.

On Aug. 3, 1953, two months after thyroidectomy, the uterus was found to be enlarged to about the size of a three and one-half months' pregnancy. A Bufo urine test was positive. On August 15 an x-ray of the chest was normal. A flat plate of the abdomen showed a normal-appearing fetus of about four and one-half months' gestation.

The patient had never been told the nature of the tumor that had been removed from her back though her husband had. She had not known that she had had a malignant growth. Now that she was pregnant Dr. Haywood felt he should tell her about the malignancy she had had and warn her of the dangers of pregnancy for her and he did so. Immediate hysterectomy was considered though the patient was very reluctant to have this done unless her life was in immediate danger.

On August 20 the author was called in consultation. So far as could be determined the patient was at about 18 weeks' gestation and her condition was normal in all respects. The fetal heart tones were normal. It had been three years and seven months since the choriocarcinoma had been removed from the spine. There was a chance that pregnancy would reactivate this malignancy but she had already passed the first four months which

is probably the most dangerous period. Therefore, it was decided to allow the pregnancy to continue and to examine her every two weeks. If she should show signs of recurrence of the malignancy a decision would be made at that time as to what treatment to give her.

She received a complete prenatal examination. A complete blood count was normal. She was type A, Rh positive. Blood Wassermann test was negative and urinalysis was normal. The blood pressure was 105/70 and her weight was 132 pounds. She was instructed in diet and was given multivitamins and mineral therapy. After her second visit it was realized that one would have to "forget" about her previous malignancy and treat her as a normal patient if any cooperation was to be gotten from her. Frequent chest x-rays were discontinued and she was told she could nurse her baby. She progressed normally in all respects though she gained 25 pounds during the pregnancy.

Her last normal menstrual period had been in April and she flowed two days in May though she could not tell me the exact dates. The baby was expected to come in January. However, she went into labor on November 29. At this time the fundus measured 30 cm. above the symphysis. The labor was twenty-four hours long though the contractions were very mild during the first twelve hours. She was delivered spontaneously after an episiotomy on Nov. 30, 1953, at the Puunene Hospital (Hospital No. K11494). The baby, a normal female weighing 5 pounds and 14 ounces at birth, appeared slightly premature, though she was able to nurse at breast and to go home on the sixth day with the mother.

The mother's course after delivery was normal in every respect. She was examined at two-week intervals during the first two months after delivery and then monthly during the first year. Pelvic examination done on Jan. 16, 1954, showed a slight cervicitis which was treated. A Bufo test on the urine was negative on Jan. 18, 1954. She nursed the baby at breast for two and one-half months. After this she dried the breasts so she could return to work in the pineapple cannery, which she did on March 1, 1954. Normal menstruation occurred in March, 1954, and has recurred every month since. She feels fine and has no pain in her back.

The baby has developed normally. She walked before she was 1 year of age and does not appear to be in any way retarded. There is a chance, of course, that the germ cells of this child were injured by the x-ray therapy the mother received before she was pregnant and that detrimental mutations were produced which will affect future generations.

Summary

This patient had a hydatidiform mole with pre-eclampsia in 1947. During the two years following evacuation of the mole she had three positive Friedman hormone tests and then one negative Friedman hormone test. The uterus remained small though she had frequent periods of excessive menstruation. Dilatation and curettage of the uterus were done on 3 occasions during the two years after evacuation of the mole but very little tissue was ever obtained. No pathological examination was made of the first two specimens. Pathological examination of the tissue from the last curettage was negative for mole tissue or choriocarcinoma. Two and one-half years after evacuation of the mole a spinal column tumor was removed which proved to be choriocarcinoma. X-ray therapy was given and apparent recovery occurred. Three and one-half years after removal of the choriocarcinoma she had a subtotal thyroidectomy for thyrotoxicosis and six months after this she delivered a normal child. Now, five years and four months after removal of the choriocarcinoma, she is apparently well.

STATUS EPILEPTICUS AND PREGNANCY

Case Report

MILTON D. KLEIN, M.D., MILTON J. GOODFRIEND, M.D., AND IRVING A. SHEY, M.D., NEW YORK, N. Y.

(From the Department of Obstetrics and Gynecology, Morrisania City Hospital, New York)

WHILE the obstetrical literature has a rather complete exposition of epilepsy associated with pregnancy, scant attention is given to status epilepticus. Since the organization of the Obstetrical Service at the Morrisania City Hospital in 1929, 2 patients were seen with this complication; both died. During this period there were 52,000 deliveries.

The prognosis of this disease when associated with pregnancy is, according to most authorities, almost always fatal.¹⁻⁴ Burnett,⁵ however, in 1946 reported the case of a primipara with status epilepticus in the thirty-third week of pregnancy who recovered after induction of labor by rupture of the membranes. The infant lived. One year later, Goodwin and Lawson⁶ observed this complication in a primipara during the first trimester of pregnancy. She survived and continued until her expected date of delivery at which time a living child was born.

Because of the seriousness of this condition and the infrequency with which it has been described the following case is reported.

Mrs. R. J., a 39-year-old primigravida, was hospitalized during the twenty-fourth week of pregnancy because of frequent and repeated convulsions.

She was first seen when six weeks pregnant. General physical and routine laboratory examinations were essentially negative. The prenatal course was uneventful until 24 hours prior to admission when she experienced several fainting spells. Epilepsy was suspected. After careful questioning, the patient admitted that she had had epileptic seizures 19 years before and had been treated at one of the "nerve clinics" for many years but in the past 2½ years had failed to return for therapy. She had been married for only one year and her husband was completely unaware of her condition. A neurologist concurred in the diagnosis of epilepsy and advised Dilantin* therapy. The following day the seizures increased in frequency and severity, necessitating immediate hospitalization.

Shortly after her admission to the hospital on Jan. 5, 1954, at 8:00 p.M. she developed repeated convulsions and remained comatose between seizures. The temperature was 100.4° F., the pulse was rapid (110) and of good volume, the blood pressure was 120/75. The heart and lungs were normal. There was no evidence of edema. The abdomen was enlarged to the size of a six months' gestation and the fetal heart tones were distant. Urinalysis, blood counts, and blood chemistry findings were within normal limits. Neurological examination failed to show any localizing signs in the central nervous system. The reflexes were rather exaggerated, there was no evidence of papilledema or signs of meningitis. A spinal tap was done and clear fluid was obtained. The initial pressure was 110 and the final pressure was 100 mm. water. Sodium Amytal was given immediately intravenously followed by Dilantin,

^{*}Dilantin (diphenyl-hydantoin sodium) manufactured by Parke, Davis & Company, Detroit, Mich.

1½ grains every four hours, and phenobarbital, 1½ grains every three hours, by Levine tube. In addition, oxygen, penicillin, and an infusion of glucose and water were administered. Between 12:05 a.m. and 10:00 a.m. on Jan. 6, 1954, she had 18 convulsions. Paraldehyde was added to the previous therapy. For the next 14 hours, despite sedation she had a convulsion almost every fifteen minutes.

On Jan. 7, 1954, the patient was transferred to the Obstetrical Service for treatment with continuous intravenous Pentothal sodium (0.3 per cent) because the usual antiepileptic therapy had failed. At this time the fetal heart tones were not audible. The patient was free of any seizures for two hours. When twitchings were subsequently noted, the rate of flow of the Pentothal solution was increased. During the next seven hours she had seven mild convulsions. At 7:30 p.m. she became very restless and was having moderately strong uterine contractions at regular 5 minute intervals lasting 30 seconds. One hour after the onset of labor she became cyanotic; the temperature was 101° F., the pulse increased to 120, and the respirations were 24 per minute; the blood pressure was 110/50. Continuous suction of the secretions of nose and throat became necessary.

Despite this therapy and although she had been free of convulsive seizures for 2½ hours, she died undelivered at 10:04 P.M. on Jan. 7, 1954.

Comment

There are several features of this case worthy of emphasis. Our patient had been an epileptic for many years and had failed to receive the benefits of continuous observation and treatment. It appears that the lack of therapy in our patient had an adverse effect on her disorder. This was manifested by epileptic seizures which within a short period after their onset became very severe, frequent, and uncontrollable. It also seems that the disease had an unfavorable effect on the pregnancy as evidenced by intrauterine death and premature labor.

As to the diagnosis, it is imperative that immediate and complete examination be made in every woman with convulsions and/or coma. Convulsive toxemia of pregnancy had to be considered. The normal blood pressure, the absence of albuminuria, and lack of edema were sufficient evidence against the presence of toxemia. Likewise, intracranial lesions such as hemorrhages and tumors may produce a similar clinical picture. The lack of focal neurological signs, the normal spinal fluid findings, and negative eye grounds ruled against such pathological conditions.

The therapy was aimed chiefly at the control of the convulsions by means of sedation. Of all the sedatives employed, the continuous intravenous Pentothal sodium solution seemed to be most effective. We regret that the Pentothal was started rather late in the course of the disorder, for it is possible that, had she received this treatment immediately upon admission to the hospital, there might have been a better chance for control of the convulsions.

The question of interruption of the pregnancy was considered when treatment failed to produce appreciable improvement after 24 hours. It was our belief, however, that the condition of the patient at all times contraindicated cesarean section or any other operative procedure. Even separation and low rupture of the membranes was impossible with a long unripe primiparous cervix.

Summary

A case of status epilepticus during pregnancy is presented; the differential diagnosis and the therapy are discussed.

References

- Sachs, E.: Monatschr. Geburtsh. u. Gynäk. 32: 649, 1910.
 DeLee, J. B.: Principles and Practice of Obstetrics, ed. 7, Philadelphia, 1938, W. B. Saunders Company.
 Greenhill, J. P.: Practitioners' Library of Medicine and Surgery, New York, 1934, D. Appleton-Century Company.
 Jardine, R.: J. Obst. & Gynaec. Brit. Emp. 12: 28, 1907.
 Burnett, C. W. F.: J. Obst. & Gynaec. Brit. Emp. 53: 539, 1946.
 Goodwin, J. F., and Lawson, C. W.: Brit. M. J. 2: 332, 1947.

REPORT OF A CASE OF SIMULTANEOUS TUBAL AND INTRAUTERINE PREGNANCIES

J. G. VIVIANO, M.D., ST. LOUIS, Mo.

(From the Department of Obstetrics and Gynecology, St. Louis University)

THE subject of concomitant intrauterine and tubal pregnancies has always been of interest because of the scarcity of cases and the diagnostic challenge which they present.

The incidence as quoted throughout the literature varies widely. Devoe¹⁴ cites 2 cases in 13,000 deliveries at the Mayo Clinic. Sprague¹ calculated the incidence at 1 in 30,000. This case is the first at St. Louis University's Hospitals (St. Mary's and Firmin Desloge) since their opening. There have been over 57,000 deliveries in these hospitals since that time. With a situation so rare, chance rather than statistics governs individual impressions concerning frequency.

Zarou and Sy¹⁰ in 1952 were able to find 10 cases reported since 1947, at which time Devoe and Pratt¹⁴ had made a similar survey. Zarou stated that, at the time of his writing, there had been 415 cases reported.

We were able to find 22 cases^{3, 6, 10, 15, 19} published since 1952. We were unable to determine the outcome in 8. We found 7 cases resulting in full-term living children, 1 with premature delivery of the intrauterine fetus, and 4 with early abortion. There were 2 cases with survival of both infants. All of these were operated upon in the first trimester for the ectopic pregnancy. Assuming the accuracy of Zarou's figures, the total number of published cases through 1954 would be 437. Schramm⁶ stated that in his survey in 1952 he was able to find only 11 reported cases where both the intrauterine and the ectopic fetuses had reached term. We were able to find 2 more, bringing this total to 13.

Case Report

The patient was a 32-year-old housewife. She was first seen on March 23, 1954, with complaints of lower abdominal cramping and low back pain. Her menstrual cycle had always been regular with 4 days of flow every 27 to 29 days. Menses had been normal in December, January, and February. There had been a menstrual period due on March 14 which did not occur. For 2 days before presenting herself for examination she had experienced some lower abdominal cramping and 12 hours before there had been a small amount of vaginal bleeding.

The physical examination showed the following: The blood pressure was 120/80. The abdomen was tender bilaterally below the umbilicus with mild rebound tenderness. The pelvic examination disclosed a bluish cervix with a softened but not enlarged uterus. There was a small amount of blood coming from the external os. To the left of the uterus was a 3 by 3 cm. acutely tender mass.

A tubal pregnancy was suspected. A Friedman test was ordered and the patient was instructed to remain in bed.

Three days later, examination showed a great decrease in tenderness. There had been little or no subjective pain since the first visit. The Friedman test was reported as negative. Two days after this there were no subjective complaints and the tenderness was gone. Seven days later, on April 5, the patient called with a severe exacerbation of lower abdominal pain.

She was admitted to St. Mary's Hospital where examination showed an acutely tender abdomen and pelvis with lower abdominal muscle spasm and rebound tenderness. There were no signs of massive concealed hemorrhage. A cul-de-sac puncture was performed and free blood which did not clot returned. At laparotomy there were 300 c.c. of clotted blood in the abdomen. The left tube contained an olive-sized enlargement in the isthmic portion with free bleeding from the fimbriated end. A simple salpingectomy was performed. The remaining pelvic organs were normal. The uterus was soft and bluish in color, but not enlarged. The corpus luteum of pregnancy was in the right ovary. We noted at the time that the right ovary was a "peculiar dumbbell shape."

The postoperative course was uneventful until the third day, when the patient vomited several times. She was watched for signs of obstruction or ileus but none developed. The vomiting subsided after 24 hours with sedation and intravenous fluids. Vaginal spotting ceased on the fourth day. On the fifth and seventh postoperative days there were similar episodes of vomiting. No physical signs of postoperative complication developed and on each occasion symptoms subsided with sedation. The patient was discharged on the ninth postoperative day.

The pathologist reported chorionic villi and decidua in the excised tube.

In the ensuing two weeks I received three telephone calls because of nausea and vomiting. On each occasion symptoms subsided with sedation.

The patient returned to the office on April 30 with no complaints other than concern over the episodes of vomiting. Examination showed the uterus to be enlarged to the size of a 6 weeks' gestation, with a typically blue cervix and globular shape. At this time concomitant intrauterine pregnancy was suspected for the first time. Re-examination two weeks later showed the growth expected with a normal pregnancy and the patient was informed of the probability.

The remainder of the pregnancy was uneventful. The patient was delivered of a normal 7 pound, 5 ounce female infant spontaneously after a two-hour labor on Nov. 20, 1954. This was the two hundred sixty-ninth day after the first day of her last menstrual period.

Assuming conception to have occurred on the fourteenth day of the cycle, the first symptoms of bleeding occurred on the twenty-third day of gestation and the laparotomy was performed on the thirty-sixth day. In retrospect we realized that the "peculiar dumb-bell-shaped ovary" which we observed on the right represented an ovary with a corpus luteum of pregnancy in either pole.

This case, in theory at least, exemplifies well the production of tubal pregnancy as a result of transmigration of the fertilized ovum with consequent growth of the blastocyst to a size too large for passage through the isthmic portion of the tube. I say this because the corpora lutea were both on the right. The tubal pregnancy was on the left and at the narrowest portion of the tube. There was no gross or microscopic evidence of chronic salpingitis which is usually thought to be the chief factor in production of tubal pregnancies.

Summary

- 1. A case of concomitant ectopic and intrauterine pregnancy is reported.
- 2. The literature concerning this subject since the last comprehensive survey has been reviewed, disclosing 22 additional cases. In 8 of these we were unable to determine the outcome. In the remaining 14 cases, the ectopic fetus was lost in 12. The intrauterine fetus aborted in 4, was delivered normally at term in 7, and prematurely in 1. In 2 cases both the extra- and intrauterine fetuses were delivered at term.

References

- Sprague, J. R., and Sprague, E. A.: J. Internat. Coll. Surgeons 16: 765, 1951.
 Derby, C. J., and Miller, R. C.: Ohio M. J. 47: 433, 1951.
 Sickenberger, P.: Am. J. Obst. & Gynec. 64: 675, 1952.
 DiPauala, G.: Prensa méd. argent. 40: 143, 1953.
 Alexander, C. A.: Am. J. Obst. & Gynec. 65: 452, 1953.
 Schramm, G.: Zentralbl. Gynäk. 74: 1984, 1952.
 Loyton, A. J.: South African M. J. 97: 661, 1052.

- Obst. & Gynec. 3: 30, 1954.

- 6. Schramm, G.: Zentralbl. Gynäk. 74: 1984, 1952.

 7. Loxton, A. J.: South African M. J. 27: 661, 1953.

 8. Rannels, H. W.: Obst. & Gynec. 2: 281, 1953.

 9. Steadman, H. E.: Obst. & Gynec. 2: 277, 1953.

 10. Zarou, G. S., and Sy, A.: AM. J. Obst. & Gynec. 64: 1338, 1952.

 11. Nandi, G.: J. Obst. & Gynaec. Brit. Emp. 60: 114, 1953.

 12. Killkenny, G. S., Gutglass, M. F., and Collins, E. G.: Obst. & Gynec. 3. Ikle, A., and Reiniger, M.: Gynaecologia 137: 17, 1954.

 14. Devoe, R. W., and Pratt, J. H.: AM. J. Obst. & Gynec. 56: 1119, 1948.

 15. Greei, P., and Duhoit: Bull. Féd. soc. gynéc. et obst. 4: 97, 1952.

 16. deOliveria: An. Clin. ginec. Fac. med. Univ. São Paulo 4: 53, 1951.

 17. Reeves, C. P., and Savarese, M. F. R.: Obst. & Gynec. 4: 492, 1954.

 18. Labry, R.: Bull. Féd. soc. gynec. et obst. 6: 71, 1954.

 19. Rossi, D.: Clin. ostet. 54: 5, 1952.

 20. Jelenek, I.: Orvosi hetil. 94: 946, 1954.

 21. Jarvinen, P. A.: Nord. med. 49: 174, 1953.

CONDYLOMA ACUMINATUM IN PREGNANCY TREATED WITH 20 PER CENT TINCTURE OF PODOPHYLLIN

Report of a Case

ANTHONY C. MILEA, M.D., NEW YORK, N. Y.

(From the Department of Obstetrics and Gynecology, St. Vincent's Hospital)

THERE are two types of papilloma of the vulva, condyloma acuminatum and the rarer true papilloma. Condyloma acuminatum is a benign growth of the vulva, warty in appearance, and distributed treelike or in patches over the vulva and contiguous structures. It forms a relatively small proportion of vulvar growths or lesions and is commoner in younger females, especially in conjunction with poor personal hygiene. The condition is caused by contamination of the vulva and is often engendered by a prolonged, irritating, and neglected vaginal discharge, frequently that from gonorrhea. The lesions multiply rapidly, and during pregnancy will usually hypertrophy and form large cauliflower-like masses in the vagina that may obstruct pelvic delivery.

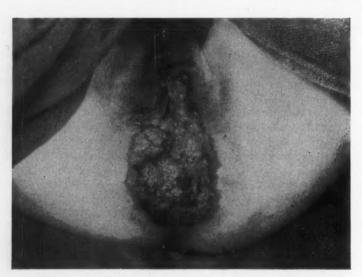


Fig. 1.—Condyloma acuminatum prior to treatment.

A. S. was a 21-year-old single white woman, approximately 27 weeks pregnant. She was admitted from the Prenatal Clinic because of a large cauliflower-like lesion arising from the perineum and posterior vaginal wall. The patient stated she had noticed this mass for about two weeks. She also complained of a foul, irritating vaginal discharge.

On admission, physical examination showed a well-developed white woman with a normally enlarged uterus of 27 weeks' gestation. Cleanliness and personal hygiene were poor. Examination of the vulva disclosed a large cauliflower-like fungating lesion arising



Fig. 2.—Biopsy showing central cylinder of connective tissue ensheathed by thick epithelial layer. The stroma shows some chronic inflammation.



Fig. 3.—Lesion following treatment.

from the perineum and posterior vaginal wall (Fig. 1). It obstructed one-half of the vaginal canal and tended to drape over the anal opening. The base was sessile. The tumor bled easily when sponged, and was characterized by a very foul, dirty gray discharge. It appeared red, necrotic, and infected, and measured 4½ inches in diameter. The remaining physical examination was negative.

The patient gave no history of gonorrheal infection. Cervical and vaginal smears were negative for the gonococcus. The Frei and Kahn tests were negative. Biopsy of the lesion showed a chronically infected papilloma. Microscopic examination showed a central cylinder of connective tissue ensheathed by a thick epithelial layer. Some degree of chronic inflammation was generally evident in the stroma (Fig. 2).

A Foley catheter was inserted into the bladder. The area surrounding the lesion was protected with a coating of petroleum jelly, and the papillomatous mass was treated with a 20 per cent tincture of podophyllin applied by cotton ball. This was done on alternate days for a total of nine treatments. At the end of this period the lesion was dry and had completely disappeared except for a few small, warty patches (Fig. 3). These were injected with 1 per cent procaine and cauterized by electric cautery in the outpatient department. While hospitalized, the patient received 5 million units of penicillin parenterally.

One month after discharge, the patient was readmitted to the Obstetrical Service, and spontaneously delivered a normal male infant. A right mediolateral episiotomy was done and repaired in the routine manner. The postpartum course was uneventful, and she was discharged on the eighth postpartum day in good condition.

Comment

Itching of the vulva and anal area and prolonged vaginal discharge are common complaints in this disease. Rarely does malignant degeneration occur. When it does, it is diagnosed by the presence of mitotic figures and invasion of the pavement epithelium. No such findings were present in this specimen.

Summary

In summary, a case is reported of a large obstructive vulvar lesion of condyloma acuminatum in a young nullipara successfully treated at 6½ months' gestation by a 20 per cent tincture of podophyllin and intramuscular penicillin. Under this therapy general clearing of the lesion ensued, thus permitting uneventful pelvic delivery.

A PUBOTRACTOR FOR INSPECTION OF THE POSTPARTUM CERVIX

R. C. CREELMAN, M.D., BREMERTON, WASH.

(From the Schutt Clinic)

THE inspection of the postpartum cervix is a valuable procedure too seldom done because of technical difficulties.

The relaxed and redundant walls of the vagina are inadequately retracted by the presently available self-retaining specula and without an assistant to apply manual retraction one seldom visualizes the postpartum cervix adequately.

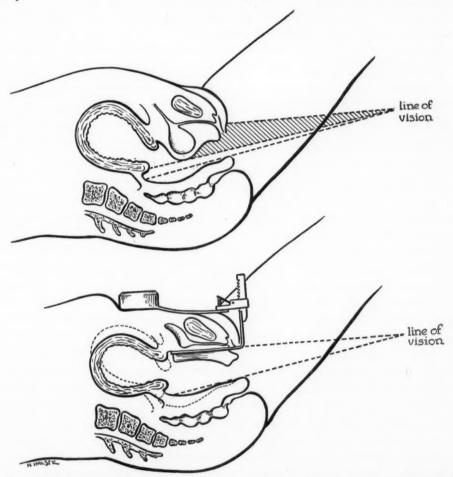


Fig. 1.—The upper illustration depicts topographical changes in the postpartum birth canal. The anterior lip of the cervix tends to be drawn anteriorly and the cervix is largely obscured by the relaxed anterior vaginal wall.

The lower illustration depicts the postpartum birth canal with the pubotractor inserted and elevated. It will be seen that visualization of the cervix is now simple and adequate. Inspection of the posterior vaginal wall for extension of mucosal lacerations and injuries of the vault is readily made with tautening of the vaginal walls and with no posterior speculum blade obscuring this area.

The existing specula retract the posterior vaginal wall, which seldom obscures the field to any extent, and attempt to retract the lateral walls, which they do with varying degrees of success. Intelligent consideration should soon make it apparent, however, that the relaxed anterior vaginal wall comprises the chief obstruction hiding the cervix.

A speculum is herein presented which, it is felt, will greatly facilitate the inspection and repair of injuries of the cervix and vault. It also reveals injuries of the perineum and posterior wall which are often obscured by the posterior blade of most of the existing specula.

This speculum departs from the customary models in being suspended from a suprapubic rest, which is weighted appropriately to enable it to retain its position without slipping. The single blade is slipped between the relatively widely spaced is chial tuberosities and into the vagina as the suprapubic blade is slid onto the lower abdomen. When the blade is fully inserted, it is approximated to the suprapubic blade and a ratchet arm connecting the two blades holds it in any degree of elevation elected.

Elevation of the anterior vaginal wall tips the cervix into a more horizontal position and it becomes clearly visible in the vaginal vault. Elevation of the anterior wall also serves to tauten the relaxed lateral walls and reduce the degree to which they protrude into the vagina and obscure visualization.

The anterior vaginal blade in its present form is a malleable ribbon which can be adapted somewhat to varying conditions. Large blades can easily be slipped over this blade to afford broader retraction.

It is felt that this speculum can be utilized in certain phases of vaginal hysterectomy to elevate bladder and ureters and further protect them.

MUSCULAR TORTICOLLIS—CONGENITAL DISEASE OR BIRTH INJURY?

GEORGE L. MOORE, M.D., BELLAIRE, TEXAS

(From the Department of Obstetrics and Gynecology, Baylor University College of Medicine)

THE condition of "congenital torticollis" or muscular torticollis involving the sternocleidomastoid muscle of the infant is afforded only passing attention by most obstetrical authors. A little more interest has been shown by pediatricians, and, logically, the most interested are the orthopedic surgeons, who see and treat these cases in relatively large numbers.

In these days of the increased threat of malpractice suits, it is important to know if this condition results from a preventable error on the part of the obstetrician, as suggested by Roemer. We should take all necessary steps to prevent any "preventable" birth injury, especially if it involves our own manipulations at the delivery table.

Greenhill² states "... [it] is not as rare as statistics show. It is often overlooked or intentionally secreted for fear of the legal responsibilty which older authors erroneously attached to it. Rupture of a healthy muscle can be brought about only by violent traction combined with extreme torsion of the head... Torticollis is usually a congenital disease..." He also states, however, "During breech deliveries, the possibility of injury must be borne in mind..."

Sippel^s wrote of hematomas forming in the muscle, causing the characteristic lump which becomes palpable in one or sometimes two areas of the muscle belly. Most present-day obstetricians believe this to be a truly stated fact.

To quote Eastman,³ "Hemorrhage into the sternocleidomastoid muscle . . . consists of an extravasation into the muscle, where it is limited by the fascial sheath. It is caused by excessive rotation of the head during delivery."

Roemer' apparently overlooked the writing of Greenhill when he stated in his article, "I have not encountered anywhere in the literature, however, the concept that the process of breech delivery causes torticollis." Actually it is inferred or stated in almost all of the obstetrical treatises, that it is a birth injury, occurring during delivery, with some "process of breech delivery" being causally related. Roemer must be commended, however, for his courage in stating that his investigation was begun after he noticed several cases in his own private practice, all in infants born by breech presentation. He also later, referring to two of his cases, stated, "These are probably hematomas which represent failure in prevention of the injury," and ". . . in reality, a birth injury, possibly preventable." He does mention, however, the possibility of laterohyperextension in utero as a possible factor. Eastman is unique in his statement that there is no association between this condition and later development of "wry neck."

A somewhat upsetting report in regard to this accepted, time-honored belief that the torticollis results from a hematoma was offered by Chandler¹ in 1948. He reported 225 cases surgically treated, 42 patients being under 1 year of age and 26 of these under 4 months of age, the youngest an infant of 3 weeks of age. Clinically, in all of these cases there was no induration of the adjacent soft parts and no reports of ecchymosis of the overlying skin. Roemer relates as evidence "... descriptions given by two mothers in which they emphasized the blue color of the tumors," but he gives no report of an obstetrician, pediatrician, or house officer making such a report.

The 42 cases in infants reported by Chandler were treated by excision of the tumor mass. Examination of the fibrous tumors of the youngest of these was of interest. They were firm, white, fusiform masses, involving part or all of the muscle belly, usually in the middle one third, limited by perimysium and separated easily from surrounding structures. In none of the specimens was there anything to suggest the formation of blood clots or residual blood pigment. Microscopic sections showed muscle fibers in all stages of degeneration, but there was no evidence of hemorrhage or residual hemosiderin, even in specimens removed in the earliest weeks of the patients' lives.

Reports consistently emphasize the frequency of associated breech delivery, 60 per cent in Roemer's study and 50 per cent in Chandler's, with the remaining cases showing a high percentage of other abnormal conditions. There were three cesarean deliveries in Chandler's group, however, and two in Roemer's, and deliveries in several of Roemer's cases were listed as low forceps, spontaneous, or unknown. There were 2 infants in Roemer's series who had apparently unrelated difficulties involving other muscles. One baby, delivered by cesarean section at seven and one-half months "also had ipsilateral equinovarus." The other, with an "easy, spontaneous delivery, had congenital spinal sclerosis' requiring several tenotomies, including one of the sternocleidomastoid."

Chandler believed that intrauterine malposition might cause ischemia as the result of pressure, leading to atrophy and shortening of the sternocleidomastoid muscle. These changes would predispose the muscle to damage with a traumatic, or even a normal delivery, which would not damage a normal muscle. Nove-Josserand and Viannay⁵ stated the middle position of the muscle was supplied by an "end artery" which became occluded. Chandler refuted this by showing in his dissections that the muscle is supplied by several arteries. An acute venous congestion with changes similar to those in Volkmann's ischemic contracture is propounded by Middleton,⁶ but Chandler has shown a profuse venous communication in the muscle, involving at least eight major veins, making it difficult to visualize any possible serious venous stasis.

Perhaps the "shearing" effect of the sternocleidomastoid muscle, however, in moving diagonally to the blood supply and overlying and moving diagonally to the underlying muscles may cause ischemia on the basis of acute passive venous congestion. This is more likely because of the easier compressibility of the veins compared to the arteries. Some interest was aroused among the pediatricians, and an article by Gruhn and Hurwitt⁴ supported Chandler's contentions. They reported upon one infant operated upon by excision of the tumor at 2 months of age. The pediatrician first noticed a mass in the neck at 9 weeks of age. Pregnancy, labor, and delivery had been "uneventful." Gross and microscopic findings were similar to Chandler's, including "no evidence of old or recent hemorrhage... vessels were patent."

They state the mass is usually detected after 10 days of age as a fusiform swelling of one side, occasionally of both. Swelling increases in size for two to four weeks, remains stationary for two to three months, and then gradually regresses. The tumor is firm and cartilaginous, not cystic or fluctuant, and does not clinically resemble a hematoma. In about one fifth of the cases, torticollis, or "wry neck," is noted in the third or fourth year of life. In different words, this means that one out of 5 of these individuals will have a resultant permanent deformity, unless it is treated. These authors conclude, "No satisfactory explanation is available for the etiology of these tumors." They close their article by stating, "It is a curious paradox that this highly controversial subject, concerning which there is so little unanimity of opinion, has evoked no recent significant contribution on the part of pediatricians, who occupy the most advantageous position from which to evaluate these lesions."

"And you, Accoucheur?"

Perhaps I was overly sensitive to criticism and the possibility of medicolegal repercussions, because the first case of torticollis in one of the breech babies I delivered occurred in an early, delicate phase of my experience in private practice. A more satisfactory explanation, to me, is the fact that I had the opportunity to intern at St. Luke's Hospital in Chicago in 1944-1945, when Dr. Chandler was treating some of his private cases which were later reported. Whatever the reason, I was startled when I received a report of "torticollis resulting from birth trauma with hematoma formation of sternocleidomastoid muscle," rendered by a pediatrician-orthopedist team, called in to treat the infant I had delivered four weeks previously. Following is a brief summary of the case.

L. D., a primigravida whose estimated date of confinement was July 11, 1953, had a relatively normal antepartum course. Her pelvic measurements were normal. Abdominal examination on June 24 had shown the fetus to be in breech presentation, so on the following visit, on July 1, an unsuccessful attempt at external version was done. An x-ray was taken on July 9, showing the fetus to be a frank breech with the sacrum to the right. There was no extreme extension of the head in any direction, although a lateral film would have been helpful. The patient was admitted to the hospital about 9 A.M. on July 20. The cervix was about 3 cm. dilated and normal contractions were occurring. Cervical dilatation was completed at 2 P.M. and the presenting part was crowning. She was taken to the delivery room and under light gas anesthesia an episiotomy was made and she was allowed to awake enough to push with the contractions. When she had delivered the baby to the umbilicus, she was again anesthetized and the baby gently extracted, with Piper forceps to deliver the aftercoming head. A resident physician assisted. The actual time of assisted delivery was four minutes. The female infant weighed 7 pounds. 14

ounces, breathed spontaneously, and was apparently in excellent condition. The pediatrician checked the baby on at least two occasions in the hospital and reported no abnormalities. When the baby was returned to the pediatrician for an examination at 4 weeks, a left torticollis was discovered, due to apparent involvement of the left sternocleidomastoid muscle. The baby was referred to an orthopedic surgeon, who planned conservative treatment for a few months, with possible surgical treatment later. The mother was dissatisfied and changed pediatricians. This pediatrician used simple massage and manipulation of the muscle, in his office, performed by him. When the baby was last seen on Aug. 12, 1954, the condition appeared completely relieved.

Comment

Noteworthy, again, is the failure of the pediatrician to observe any acute evidence of trauma, such as ecchymosis, etc., on repeated examination of the baby in the hospital. Also, the striking results of conservative therapy are seen; it should be remembered that 4 out of 5 patients recover spontaneously. X-ray showed no extreme malposition of the head prior to labor, but of course it may have been in extreme lateral extension during labor.

It is unlikely that a conscientious physician like Roemer could possibly tear a normal muscle and cause a hematoma, as he reported with his last two cases, while trying desperately to avoid such a happening.

In summary, suffice it to say that although we do not know the exact etiology of the condition, we know that the lump in the muscle is not the result of a hematoma, and the injury is not primarily iatrogenic.

References

- i. Chandler, F. A.: J. Bone & Joint Surg. 30: 566, 1948.
- DeLee, J. B., and Greenhill, J. P.: Principles and Practice of Obstetrics, ed. 8, Philadelphia, 1943, W. B. Saunders Company, p. 854.
 Eastman, N. J.: Williams Obstetrics, ed. 10, New York, 1950, Appleton-Century-Crofts,
- Inc., p. 995.
- 4. Gruhn, J., and Hurwitt, E. C.: Pediatrics 8: 522, 1951.

- 6. Middleton, D. S.: Brit. J. Surg. 18: 188, 1930.
 7. Roemer, F. J.: Am. J. OBST. & GYNEC. 68: 1146, 1954.
 8. Sippel: Ztschr. Geburtsh. u. Gynäk. 84: 790, 1922.

SUCCESSFUL POSTMORTEM CESAREAN SECTION

JOHN V. KELLY, M.D.,* GROSSE POINTE, MICH., AND HEBERT G. WINSTON, M.D., SCARSDALE, N. Y.

(From the Division of Obstetrics and Gynecology of the Metropolitan Hospital and the New York Medical College, New York, N. Y.)

POSTMORTEM cesarean section is a rare occurrence in medical practice and is successful even less frequently. It is the purpose of this paper to give a brief review of its history and incidence, and present two case reports with the purpose of emphasizing the importance of this rare procedure when the occasional opportunity arises.

Postmortem cesarean section was probably the first major surgical operation undertaken in the history of mankind. Successful procedures of this type are narrated in the legends of the Romans, probably because the Roman Law of Numa Pompilius decreed that any woman who died during pregnancy should have her child removed from the abdomen prior to her burial. Graham, in his history of gynecology and obstetrics, relates that such famous names as the mythical Bacchus, the philosophers Gorgias and Trismegistes, the soldier Scipio Africanus, and the physician Asklepios, delivered by his father Apollo from the womb of the dead Koronis, were all products of this successful procedure.

Published articles and reports of this operation have been collected from as far back as the eighteenth century. In an excellent review, Duer² in 1879 reported a total of thirty-six successful postmortem cesarean sections during the eighteenth and nineteenth centuries. We have collected an additional seventy-five cases from the literature of the twentieth century.

TABLE I. CAUSES OF MATERNAL DEATH IN 111 POSTMORTEM CESAREAN SECTIONS WITH INFANT SURVIVAL

CAUSE OF DEATH	NUMBER OF CASES
Eclampsia	39
Tuberculosis	31
Cardiac	7
Hypertensive cardiovascular disease	5
Rheumatic heart disease	2
Accident (traumatic skull fracture, etc.)	5
Pneumonia (plus pneumococcic meningitis, 1)	4
Aneurysm	$\frac{4}{3}$
Dissecting aneurysm	2
Ruptured syphilitic aneurysm	1
Spinal anesthesia	3
Bulbar poliomyelitis	2.
Cholera	2
Peritonitis (fulminating, etiology unknown)	1
Gangrene of the neck	1
Unknown	13
Total	111

Present address, Allmänna Barnbordshuset, Stockholm ö, Sweden.

The total number of reported successful postmortem cesarean sections in the available world literature is one hundred and eleven cases. These cases and the respective causes of death are listed in Table I. To these cases we wish to add two case reports, which describe our experiences with this problem.

CASE 1.—A. R., a 30-year-old gravida ii, para 0, Puerto Rican woman, was first admitted to Metropolitan Hospital on April 12, 1952, in acute congestive heart failure and with evidence of small pulmonary infarction and residual evidence of subacute rheumatic activity. The diagnosis by our cardiologist was rheumatic heart disease with mitral insufficiency and stenosis, enlarged heart, regular sinus rhythm, and congestive heart failure, Class III. She was placed on digitalis, mercurial diuretics, sodium restriction, bed rest, and antibiotics, and responded well enough to treatment to be discharged on May 12, 1952. She did fairly well on our Home Care Service until Aug. 28, 1952, when mild failure again supervened and she was readmitted to the hospital service. It was learned at that time that she was pregnant, her last menstrual period having occurred on April 14, 1952. Adjustment in the dosage of digitalis resulted in some improvement in the cardiac status. The attending physicians on the medical service advised interruption, but the patient and her husband would not permit interruption of the pregnancy on religious grounds. Rigid management, including digitalis, mercurial diuretics, sodium restriction, absolute bed rest, and close cooperative management with the medical service were maintained.

At the time of admittance, the physical examination showed a well-developed, wellnourished Puerto Rican woman who appeared to be in moderate distress. The respirations were 24 per minute and a slightly productive cough was present. The radial pulse and apex rate were 120 per minute at bed rest, there was a one plus pretibial and sacral edema with moist post-tussive râles at the left base. The blood pressure was 110/80. The heart was enlarged both to the right and to the left, while a harsh systolic and a presystolic apical murmur were present. The liver was palpated 4 fingerbreadths below the right costal margin. The uterus was enlarged to approximately 41/2 months' size. A chest x-ray revealed moderate enlargement of the heart in all diameters with accentuation of the pulmonary conus segment and some pulmonary congestion. The blood serologic test for syphilis was positive. blood group was A and the Rh factor was positive. The cardiac regime was augmented by the utilization of intramuscular aminophylline, more frequent mercurial injection, and intermittent ammonium chloride therapy. A course of antisyphilis therapy was instituted with the use of penicillin G. The patient improved but intermittently developed signs and symptoms of incipient cardiac decompensation. An increase in digitalis dosage was abandoned due to manifestations of toxicity.

The patient's progress was relatively satisfactory until she was about 30 weeks pregnant when again incipient failure occurred. In an effort to ensure a more rigid sodium restriction, a rice diet was instituted. This resulted in some improvement in her body status. Her weight gain had been held to approximately 8 pounds. On Dec. 20, 1952, a 2 pound weight gain in 24 hours was noted. Mercuhydrin, 2 c.c., was immediately given intravenously. Three hours later respiratory distress became more marked and frank pulmonary edema appeared. She was approximately 32 to 33 weeks pregnant at this time.

Vigorous therapeutic measures were instituted in collaboration with the medical service, including pressure oxygen by mask, morphine, aminophylline, 50 per cent glucose intravenously, dry phlebotomy, and wet phlebotomy (500 c.c.). Pressure oxygen through alcohol, by the technique of Luisada, was instituted and while some improvement occurred it was not marked and was only transient. Imminence of fatal outcome was obvious and preparations for agonal cesarean section were made. Within 45 seconds after death had been pronounced by three physicians, a 1,500 gram depressed female infant was delivered by classical cesarean section. Resuscitation was successful and the baby was transferred to the prepared incubator. The baby progressed well and now at 3 years of age is a normal healthy little girl.

A postmortem examination of the mother was performed and revealed rheumatic heart disease, mitral stenosis with a very tight orifice, pulmonary edema, old pulmonary infarction, and chronic passive congestion of the liver, spleen, and kidneys.

Case 2.—B. O., a 37-year-old Negro woman, gravida v, para ii, who had had 2 abortions, was first seen in the Metropolitan Hospital Obstetrical Clinic on Aug. 25, 1954. Her last normal menstrual period had been on Jan. 14, 1954. The chief complaints were increasing dyspnea for three months and the presence of a "lump" in the neck and a "big lump" in the breast also present for three to four months, for which she had sought treatment from two local "doctors" without success. The patient was immediately admitted to the Metropolitan Hospital for diagnostic workup and therapy.

The positive physical findings included the presence of a 4 cm. hard right supraclavicular node, a nodular, indurated 10 cm. mass in the left breast, large distended veins covering the anterior chest, rhonchi and coarse râles throughout the lung fields, a uterus enlarged to the size of a 7 to 7½ months' pregnancy, a regular fetal heart rate of 144 in an orthopneic 175 pound Negro woman.

The diagnostic hospital workup included biopsies of the right supraclavicular node and left breast mass, both of which showed small-cell carcinoma of the breast; chest x-rays which showed mediastinal widening, at electasis of the base of the left lung, extensive irregular densities in both lung fields and pulmonary congestion, and a single fetus of approximately 7 to 7½ months' size.

Surgical and radiological consultants agreed that the extent of the neoplasm was too great to undertake specific therapy for it, so the treatment consisted of bed rest, sedation, oxygen via tent as needed, usually 2 to 3 hours each day, and prophylactic antibiotics. The patient's condition improved symptomatically on this treatment and during the next four weeks she was comfortable and relatively asymptomatic save for occasional bouts of dyspnea and hemoptysis which were treated with oxygen and aminophylline. She was also known to have had asthma for six years. During this time in the hospital, equipment for agonal cesarean section was always readily available in case of sudden demise. The plan of therapy included allowing the gestation to proceed to approximately 38 weeks, if possible, to provide maximal chance for survival of the fetus, at which time the patient was to be delivered by elective cesarean section followed by a surgical castration to be performed at the same time, with a course of palliative deep x-ray therapy to follow.

However, on Sept. 25, 1954, at exactly 36 weeks of gestation, the patient's condition suddenly began to deteriorate and over a period of 4 hours increasingly severe dyspnea and hemoptysis rapidly developed which did not respond to vigorous therapeutic methods, including pressure oxygen by mask passing through alcohol after the technique of Luisada, morphine, aminophylline, 50 per cent glucose intravenously, and dry and wet phlebotomy (600 c.c.). Despite the attempts to control the acute pulmonary edema, the patient died. After death was pronounced by three physicians, a rapid classical cesarean section was performed and a depressed 2,160 gram female infant was delivered 3 minutes after the patient's demise. Resuscitation with suction and oxygen by the intratracheal method was rapidly successful, the baby cried and breathed spontaneously within two minutes of delivery, and was transferred to the prepared incubator. She is presently 18 months old and appears to be a normal healthy baby.

A postmortem examination was performed on the mother and revealed massive pulmonary edema, small-cell carcinoma of the left breast and metastases throughout both lungs and to the mediastinum, pericardium, diaphragm, the liver, and both ovaries. The placenta was negative for metastases.

Comment

The rare success in the past with postmortem cesarean section has led to opinions that the procedure is not justified. The pessimism with which it is described by Sullivan and his group³ and Eastman,⁴ however, does not coincide with our experience. It is our contention that a more enthusiastic attitude toward postmortem cesarean section is indicated today because of the improved

methods of infant resuscitation and care of premature infants which have contributed to an increased fetal salvage rate. Eastman⁵ made note of the infrequency of survival of the baby when death of the mother is due to chronic wasting diseases, especially when the terminal stage is associated with cyanosis. Greenhill⁶ likewise commented on the greater frequency of a successful result when the maternal death is due to acute conditions. It is precisely in the less acute situations, however, that opportunity to perform the operation is more likely to occur and adequate preparation for the procedure including incubator and resuscitation equipment can be made available.

The stipulation has been made that the operation should not be done if the husband's permission has not been obtained. Greenhill quoted Bacon as having proved that permission is not necessary, although he stated its desirability. Lattuada and Whiteside discussed the medicolegal aspects and convincingly asserted the necessity of performing the procedure even despite the husband's refusal of consent. They also raised the question whether the physician is morally, if not legally, culpable in not performing the operation. The article of Lattuada contains an interesting discussion of this aspect of the problem and is highly recommended. One statement in particular is impressive: "No individual has the right to deliberately and intentionally take the life of another or to deprive another of the right to live. The obligation to save human fetal life, when it can be done without destroying or jeopardizing another life, is absolute."

Summary

Postmortem cesarean section has been reviewed. One hundred and eleven successful postmortem cesarean sections have been collected from the world literature since the eighteenth century and a tabulation of the causes of maternal deaths has been detailed. The history of the operation has been briefly presented. The necessity for the more frequent performance of the operation has been outlined and the medicolegal aspects have been discussed. Two additional and illustrative cases of successful postmortem cesarean section are presented from our obstetrical experience at the Metropolitan Hospital.

We wish to express our gratitude to Dr. Clair E. Folsome for his suggestions and encouragement.

Bibliography

- 1. Graham, H.: Eternal Eve, New York, 1951, Doubleday & Company, Inc.

- Graham, H.: Eternal Eve, New York, 1951, Doubleday & Company, Inc.
 Duer, E.: Am. J. Obst. 12: 1, 1879.
 Sullivan, C. L., Minkel, H., Campbell, E., and Graham, J.: Postgrad. Med. 14: 329, 1953.
 Eastman, N. J.: Williams Obstetrics, ed. 10, New York, 1950, Appleton-Century-Crofts, Inc.; editorial comment, Obst. & Gynec. Surv. 4: 665, 1949.
 Eastman, N. J.: Editorial comment, Obst. & Gynec. Surv. 6: 538, 1951.
 Greenhill, J. P.: Principles and Practice of Obstetrics, ed. 9, Philadelphia, 1947, W. B.
- Saunders Company.
 7. Lattuada, H. P.: Am. J. Surg. 84: 212, 1952.
- 8. Whiteside, G. W.: Am. J. Obst. 73: 105, 1916.

References for Remainder of Case Reports

- Bacon, C. S.: Surg., Gynec. & Obst. 12: 168, 1911.
 Baden, E. E., and Baden, W. F.: Am. J. Obst. & Gynec. 66: 202, 1953.
 Bohmer, J.: Doctor's thesis, Berlin, 1908, R. Treukel.

- Campbell, A. M., and Miller, J. D.: J. Michigan M. Soc. 30: 923, 1931.
 Chamorro, T.: Semana méd. 2: 733, 1942.
 Chappaz, G., and Dazy, R.: Bull. Assoc. gynéc. et obst. 2: 415, 1950.
 Dobbs, E. H.: West Virginia M. J. 44: 80, 1948.
 Fallon, M. J.: Boston M. & S. J. 195: 929, 1926.
 Ghose, S. K.: Calcutta M. J. 37: 303, 1940.

- 9. Ghose, S. K.: Calcutta M. J. 37: 303, 1940.
 10. Harrar, J.: Am. J. Obst. Bull. Lying-In Hosp. N. Y. 73: 1046, 1916; 10: 218, 1916.
 11. Harrison, D. A., Shelton, J. H., and Carrithers, C. M.: J. A. M. A. 110: 2066, 1938.
 12. Heppner, M.: J. A. M. A. 72: 727, 1919.
 13. Hoffman, P.: West Virginia M. J. 31: 78, 1935.
 14. Holden, R. T.: M. Ann. District of Columbia 1: 63-64, 1932.
 15. Johnson, R. O., and Frank, T. V.: Am. J. Obst. & Gynec. 53: 343, 1947.
 16. Kerr, Munro J. M., and Moir, J. C.: Operative Obstetrics, Baltimore, 1950, Williams & Wilkins Company.
 17. Kronick, M.: New England, I. Med. 243: 953, 1950. Wilkins Company.

 17. Kronick, M.: New England J. Med. 243: 953, 1950.

 18. Kupfer, K.: Doctor's thesis, Leipzig, 1927, E. M. Löffler.

 19. Lacomme, L.: Bull. Soc. gynéc. et obst. 28: 393, 1939.

 20. Linzenmeier, G.: Med. Klin. 16: 439, 1920.

 21. Meneghini, T.: Atti. Soc. ital. di ostet. e gynec. 35: 320, 1939.

 22. Moran, R. J.: New England J. Med. 227: 988, 1942.

 23. Moran, T. A.: J. Iowa M. Soc. 31: 195, 1941.

 24. Morgan, J.: Lancet 2: 132, 1940.

 25. Oldfield, O.: J. Obst. & Gynaec. Brit. Emp. 28: 570, 1921.

 26. Pfaff, O. G.: Trans. Am. A. Obst. & Gynec. 29: 42, 1916.

 27. Phaneuf, L. G.: Am. J. Surg. 35: 446, 1937.

 28. Presnell, G.: J. Missouri M. A. 39: 177, 1942.

 29. Purdie, A. W.: Gen. Practitioner 15: 347, 1945.

 30. Rider, F.: Nebraska M. J. 16: 474, 1931.

 31. Roberts, H. G.: Brit. M. J. 1: 829, 1925.

- Purdie, A. W.: Gen. Practitioner 15: 347, 1945.
 Rider, F.: Nebraska M. J. 16: 474, 1931.
 Roberts, H. G.: Brit. M. J. 1: 829, 1925.
 Roemer, H.: Zentralbl. Gynäk. 62: 295, 1938.
 Rosin, I.: Lancet 1: 820, 1927.
 Rutherford, N. J.: Glasgow M. J. 128: 12, 1937.
 Schopps, M.: Berl. klin. Wchnschr. 55: 221, 1918.
 Schwartz, J.: Am. J. Obst. & Gynec. 62: 539, 1951.
 Simmons, J. M., and Ellis, H. B., Jr.: Am. J. Obst. & Gynec. 57: 604, 1949.
 Sproull, O. T.: Ohio M. J. 13: 169, 1917.
 Stone, M. J.: New York M. J. 118: 571, 1923.
 Talisman, M. R.: Am. J. Obst. & Gynec. 68: 717, 1954.
 Tietsze, K.: Med. Welt. 9: 1077, 1935.
 Titus, P.: The Management of Obstetric Difficulties, ed. 3, St. Louis, 1945, The C. V. Mosby Company.
- Mosby Company.

 43. Torpin, R.: Treatise on Obstetrical Labor, Augusta, Ga., 1948, Obstetrical and Gynecological Book Co., p. 498.

 44. von Seuffert, E.: Arch. Gynäk. 82: 725, 1907.

 45. Walker, A. H. C., and Matthews, S.: Brit. M. J. 1: 938, 1950.

 46. Weil, A., Yoder, R., and Bachand, M.: Am. J. Obst. & Gynec. 66: 207, 1953.

 47. Wheeler, H. E.: Northwest. Med. 21: 165, 1922.

 48. Yule, G. W.: Edinburgh M. J. 33: 49, 1926.

AN UNUSUAL CASE OF EXUDATIVE VAGINITIS (HYDRORRHEA VAGINALIS) TREATED WITH LOCAL HYDROCORTISONE

LEWIS C. Scheffey, M.D., A. E. Rakoff, M.D., and Warren R. Lang, M.D., Philadelphia, Pa.

(From the Department of Obstetrics and Gynecology, Division of Gynecology, Jefferson Medical College and Hospital)

THIS report concerns an instance of a rare type of vaginitis of unknown etiology characterized by extreme chronic inflammation, membrane formation, and a copious thin vaginal discharge which responded remarkably to local hydrocortisone therapy. Vaginitis of this type has been referred to as exudative or membranous vaginitis, hydrorrhea vaginalis, and serofibrinous allergic dysregulative colpitis.¹

Case Report

M. P., white, aged 50 years, gravida ii, para ii, first consulted one of us (L. C. S.) in April, 1954, by referral from Dr. H. B. Harris of Kingston, Pa. The patient's chief complaint was that of profuse, clear, serous discharge, which was estimated to measure more than a cupful daily. This had been present since the fall of 1953 and was attributed to the use of a proprietary douche powder that the patient thought might have been "too strong." The preparation was stated to contain boric acid, aluminum and potassium sulfate, oxyquinoline sulfate, menthol, thymol, phenol, eucalyptol, salicylic acid, and methyl salicylate. Several months after the onset of the discharge, the patient noted bilateral ankle edema gradually progressing to the level of the knees. Many local medications, including various antibiotics, had been used in an effort to eradicate the annoying leukorrhea. Dilatation and curettage, cervical biopsy, and cauterization had been performed elsewhere in October, 1953; pathologic reports at that time were "chronic cystic cervicitis" and "minimal endometrium." A repeat dilatation and curettage was done at a second hospital in February, 1954, and "chronic endometritis" and "atrophic endometrium" were diagnosed. No improvement was noted following any of the therapeutic measures previously utilized. The past medical history of this patient was not significant otherwise.

At the time of the first visit to the senior author, pelvic findings were as follows: the vagina was inflamed and covered with a whitish membranous exudate. There was a copious amount of serous discharge, light brown in color. The vaginal tissues seemed hard and rigid and the vulva was secondarily inflamed. The corpus was normal in outline, size, and position, and the adnexal areas were negative. Rectal examination was normal. Inguinal adenopathy was absent. Urinalysis of a catheterized specimen was negative. Wetsmear examination of the vaginal secretion showed many basal and white cells, and the gram-stained smear demonstrated many leukocytes and occasional gram-positive cocci. Smears for cytologic examination showed a serous exudate with relatively few squamous epithelial cells. There were many small, round cells with dark-staining nuclei and scant cytoplasm, smaller, rounder, and darker than the usual endometrial cells. The possibility of ovarian origin was considered. A vaginal culture under micro-anaerobiosis was negative for Neisseria gonorrheae; the predominating organisms on chocolate agar were a gramnegative rod resembling a "rough coli formed" bacillus or Bacteroides, yeast cells, alpha hemolytic streptococci, and Neisseria catarrhalis.

Volume 72 Number 1

The patient was then admitted to the Jefferson Medical College Hospital on June 18, 1954, for more thorough evaluation. The following studies were done and were within normal limits: repeat urinalysis of a catheterized specimen, blood sedimentation test, phenolsulfonphthalein excretion, plasma proteins, and fasting blood sugar determinations, basal metabolic rate, chest x-ray, electrocardiogram, and cystogram. Two complete blood counts were normal except for moderate eosinophilia (8 and 10 per cent). Wassermann and Frei tests were negative as was the test for Bence Jones protein.

B.

Fig. 1.—A, Cytologic smear before treatment. Note numerous round and inflammatory cells and lack of squamous cels. B, Cytologic smear after one month of therapy with local hydrocortisone. Note absence of inflammation and the presence of normal-appearing superficial squamous cells.

The patient was then seen in consultation by an internist (Dr. L. Tocantins) who found no systemic disease but suggested that the edema of the legs might possibly be due to protein loss per vaginam. A urologist (Dr. T. R. Fetter) found no evidence of a urinary fistula.

As before, repeat gram-stained smears showed gram-positive cocci and rods. Cultures of the vaginal fluid for fungi and acid fast bacilli were both negative. No Donovan bodies were found in the vaginal exudate. Repeat cytologic smears were loaded with leukocytes in such large numbers that the other cells were almost obscured. There was much degeneration, debris, and evidence of blood; a few clumps of swollen basal-layer cells were noted. A few groups of very small cells of questionable origin with dark-staining nuclei were still seen (Fig. 1, A). A leukocytic differential count on these cytologic smears revealed 25 per cent of the white cells to be presumably eosinophils.

On July 3, 1954, a repeat dilatation and curettage with multiple cervical biopsies were carried out, and random vaginal biopsies were also taken. Pathologic reports disclosed "chronic cervicitis" and "chronic vaginal ulcer" (Fig. 2). No specific diagnosis could be made on the scant curettings obtained.

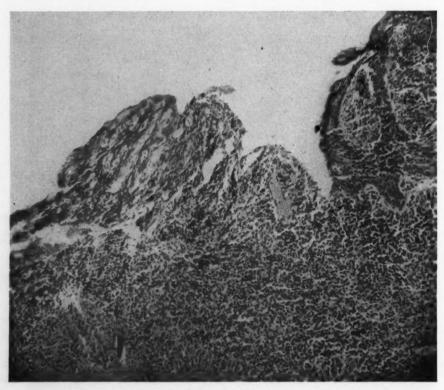


Fig. 2.—Vaginal biopsy showing loss of vaginal surface epithelium except in one area. Diffuse inflammation is also present.

Since the patient showed evidence of a chronic vaginal inflammatory condition, with infiltration by round cells and a high proportion of eosinophils, it was thought worth while to test the effect of local hydrocortisone therapy. This was considered safe since the bacteriologic and histologic studies were negative for tuberculosis. The patient was, therefore, given 10 mg. tablets of hydrocortisone* to be used intravaginally three times daily. This was begun on July 8, 1954.

^{*}Cortril, Pfizer Laboratories (glycerin monostearate, 25.5 mg., carbowax 4000, 510.0 mg.; carbowax 6000, 727.0 mg.; magnesium stearate, 12.5 mg.; hydrocortisone, 10 mg.).

Seven days later, the discharge and inflammatory induration had diminished considerably, and the patient was discharged from the hospital for interval observation. The dose of hydrocortisone was slowly decreased until one month later the patient was using only 5 mg. daily. Since the original symptoms were so severe, this therapy was continued for several months after which daily lactic acid douches were advised. The improved state of the cytologic smear after one month of therapy with hydrocortisone is shown in Fig. 1, B. Since then the patient has continued to do well.

Comment

A satisfactory explanation for the chronic exudative type of vaginitis described in this case report is still forthcoming. The possibilities which were considered most likely during the course of the study were a chronic infectious process such as tuberculosis, actinomycosis, some other granulomatous lesion, or a chronic sensitivity reaction. The bacteriologic, histologic, and other laboratory studies failed to confirm a specific infection, nor were the clinical findings and course typical of any such lesions. Favoring, but by no means proving, an "allergic" type of reaction as the etiological factor, were the eosinophilia, the high proportion of eosinophils in the exudate, and the remarkable response to hydrocortisone. It is well known that the corticoids may produce a "disappearance" of an inflammatory exudate, but one would then expect further spread of the disease due to breakdown of these local barriers.

We could discover but one similar case report in the literature. This was a chronic type of exudative vaginitis occurring in a girl of 12 who presented vaginal findings resembling those of the patient described. Blood eosinophilia was also present and histologically some epithelial vacuolization was found. The child was treated successfully with a local estrogenic preparation. It was postulated by the authors that the estrogen inhibited hyaluronidase and thereby decreased tissue permeability. Although this case resembles the one herewith presented by us, we were unable to demonstrate epithelial vacuolization; in fact, the degree of ulceration was so marked that there was but little epithelium found on the multiple vaginal biopsies studied.

Clarke and Selve, working with ovariectomized and immature rats, have reported that many hormonally active steroids, including hydrocortisone, stimulate the vaginal epithelium to undergo varying degrees of stratification, cornification, or mucification. It might be that estrogen and hydrocortisone share properties influencing tissue permeability and vaginal cornification which would be helpful in treating the type of vaginitis we have described.

Summary

A case of a rare type of severe chronic vaginitis of unknown etiology is presented, characterized by a profuse serous discharge, adherent vaginal membrane, blood eosinophilia, and a high concentration of eosinophils in the vaginal exudate. No causative organisms could be demonstrated; the possibility of allergic factors was considered but not proved. The vaginitis responded remarkably to the local use of hydrocortisone after having been resistant to many other types of treatment.

References

Franken, H., and Rotter, W.: Geburtsh. u Frauenh. 14: 154, 1954.
 Clarke, E., and Selye, H.: Am. J. M. Soc. 204: 401, 1942.

AGENESIS OF MULLERIAN DUCTS WITH REPORT OF CASE*

ROY L. GROGAN, M.D., FORT WORTH, TEXAS, AND TRUMAN C. BLOCKER, M.D., GALVESTON, TEXAS

(From the University of Texas Medical Branch)

THE fact that the uterus and vagina normally are formed by the fusion of two tubelike structures makes possible many departures from the usual configuration. It seems remarkable that a perfect reproductive system is to be found more often than any departure from the usual normal development. Since the superior portions of the Müllerian ducts which do not fuse and which develop into the ovaries and Fallopian tubes are less often affected than the lower portions, it is of interest to note that there has been no record of a uterus having been found without at least one or both Fallopian tubes attached to it. It is true, though, and has been observed in frequent instances, that both Fallopian tubes may be present without evidence of a uterus. In such cases the tubes usually end blindly without reaching the midline. They may, however, extend the full length of the vestigial uterus which may be either unicornate or bicornate, and fuse at the level of the bladder. It has been stated that no lack of fusion of the Müllerian ducts occurs without some abnormality of the genitourinary tract; it has also been observed that with bilateral renal agenesis there was associated absence of uterus, cervix, and most of the vagina, although the Fallopian tubes and ovaries or ovary are present.

Miss B. S., a 19-year-old girl, a college student, was referred to me from a West Texas town for the purpose of diagnosis and with the statement that she had never menstruated and there was no obvious vaginal outlet. At the time of admission she was complaining of abdominal cramps and amenorrhea. The only operation she had previously had was tonsillectomy and adenoidectomy.

According to the previous history, it had been called to the attention of this young woman, by her mother, that her genitals did not seem to be perfectly normal. She was sent to the referring doctor who did not find any entrance to the vagina and could not determine the presence of a uterus. A careful examination was made, and, according to the findings, there was congenital absence of the entrance to the vagina and a fibrous mass high in the pelvis posterior to the bladder. She also complained of an acute abdominal pain in the right lower quadrant which was diagnosed as chronic appendicitis.

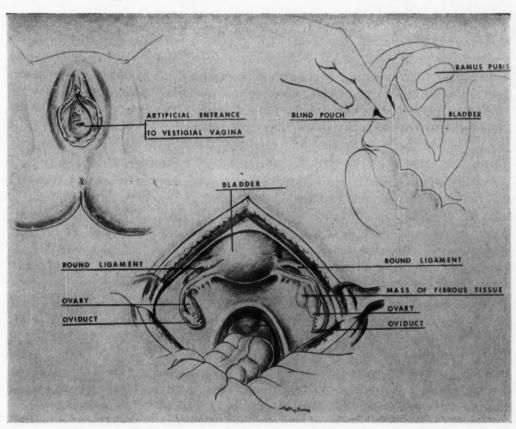
With the permission of the family, she was hospitalized and operated upon. The entrance to the vagina was found to be only a dimple, so a transverse incision was made below the anterior urethra after overdistending the bladder (Fig. 1, A and B). This was separated by blunt dissection with the gauze-covered finger, and the pouch was found to be about $1\frac{1}{2}$ to 2 cm. in depth. Afterward, a midline incision was made in the abdomen and the contents viewed from above. It was found that there was a fibrous mass, possibly 2 cm. in each dimension, into which, or from which, there radiated to each side of the pelvic wall a ribbonlike mass near the end of which there was an ovary and a partially developed Fallopian tube. The right ovary was also attached to a fibrous mass which was excised and sent to the laboratory for diagnosis (Fig. 1, C).

^{*}Presented at a meeting of the Texas Association of Obstetricians and Gynecologists, Houston, Texas, Feb. 26, 1955.

After this investigation was made and the appendix was removed, the abdomen was closed in the routine manner and diagnosis from the pathological laboratory was awaited. The laboratory reported that there was a congenital deformity with chronic appendicitis and fibroma of the right ovary. There was no evidence of a uterine mass but a fibrous mass was in the posterior portion of the pelvis behind the bladder and from this there radiated the two ribbonlike rudimentary or vestigial remains of the uterus, indicating that there was a lack of fusion of the Müllerian ducts. The patient had an uneventful recovery.







C.

Fig. 1.—A, Artificial entrance to vestigial vagina with bladder distended. B, Blind pouch indicating absence of fusion of the vaginal canal. C, Distended bladder showing insertion of ligaments, oviducts, and ovaries.

She returned to her collegiate studies and activities but was advised that when there was a possibility of her getting married an artificial vagina might be constructed, inasmuch as the patient was having symptoms of menstruation, such as malaise and soreness of the breasts each 28 days. She was not examined subsequently until January, 1954, when from a Guidance Center a request was made for her history. The statement was also made that she was having some emotional upset due to "difficulty she is having in her interpersonal relationships, and the feeling her anatomical deficiency was having a strong bearing upon her problem." She was then referred to Dr. Truman G. Blocker of the University of Texas Medical Branch, for corrective treatment. According to information received later, she underwent a successful operation.

B

Comment

During the past fifteen years we have treated on our service at the University of Texas Medical Branch a total of 13 patients with complete congenital absence of the vagina and a fourteenth patient with atresia of the first portion of the vagina. The procedure of choice, which we have used in every instance, we believe to be the inlay graft technique which has been popularized by McIndoe and Counseller of the Mayo Clinic. Here a channel is made between the bladder and rectum by blunt dissection if possible, with a catheter in the bladder as a guide. The cavity is made as large as possible to allow for later Thick-split skin grafts are attached with dermatome glue to a ready-made prosthesis (about 10 by 4 cm.), which has the upper end slightly larger than the remaining portion in order to hold it in place more securely. The edges of the labia are freshened and sutured over the end of the mold to hold it in place until sufficient time has elapsed for take of the graft. A Tbinder and pad are worn for several days after operation to absorb drainage from the area, and during this time the catheter is left in place with appropriate prophylactic antibiotic therapy for prevention of urinary tract infections.

Following operation, patients are given a conformer to be worn for several months until maximum shrinkage of the tissues occurs. We have employed a number of different materials as vaginal conformers: Pyrex glass, acrylic dental compound, and finally balsa wood, which we have used in the last several cases. We pad it first with sponge rubber, held in place with dermatome glue, to prevent excessive pressure on the rectovaginal septum, and cover the entire prosthesis with an ordinary latex condom.

Because of the frequency of urinary as well as uterine abnormalities associated with congenital vaginal atresia and because of the emotional crises which may occur when deformities are not discovered until late adolescence, perhaps at the time of a premarital examination, we feel that the optimum time for vaginoplastic operations is in early adolescence. At this time emphasis can be placed upon deviations from the normal menstrual pattern. Also, the parents and gradually the patient can be prepared for the likelihood of sterility in marriage. Of course, when operation is performed early, dilatation should be carried out at regular intervals.

We have been very well satisfied with the results of surgery using the McIndoe-Counseller technique, both from the standpoint of postoperative followup and from reports of patients with regard to happy marriages and well-adjusted personalities in general.

References

- Counseller, V. S.: J. A. M. A. 136: 861, 1948. Holmes, W. R.: Tr. South. S. A. (1947) 59: 406, 1948. Hunter, R. H.: Contrib. Embryol. 22: 91, 1930.
- Contrib. Embryol. 24: 61, 1931. Koff, A. K.:
- McIndoe, W. M.: Arch. Soc. cirujanos, Chile, p. 83, 1950.
 Patten, Bradley M.: Human Embryology, ed. 2, New York, 1953, McGraw-Hill Book Company, Inc.
- Potter, Edith L .: Pathology of the Fetus and the Newborn, Chicago, 1952, The Year Book Publishers, Inc., pp. 383-390.

Department of Reviews and Abstracts

EDITED BY LOUIS M. HELLMAN, M.D., BROOKLYN, N. Y.

Review of New Books

Premature Infants. By Ethel C. Dunham. Second edition. 459 pages with 78 illustrations. New York, 1955, Paul B. Hoeber, Inc. \$8.00.

Like the first edition of her book, Dr. Dunham has presented a complete and well-documented discussion of premature infants. Many excellent photographs, tables, and graphs illustrate the text. Parts I and III, dealing with general considerations and public health aspects of prematurity, are particularly recommended.

The second portion, dealing with clinical considerations in the care of premature infants, suffers from too much documentation and not enough apparent intimacy with subjects discussed. While pages are devoted to discussion of gastrointestinal anomalies, only four sentences are given to the much more common problem of inguinal hernia. Recommendation for palliative measures alone is not in keeping with present thought on the care of such infants. The discussion of retrolental fibroplasia is good, but the only recommendations for oxygen concentration in the appendix suggest initial oxygen concentrations of 40 to 50 per cent. This is not in keeping with current thoughts on therapy. Erythroblastosis fetalis due to ABO blood incompatibility is stated to be relatively rare. This is questioned.

Festschrift zum 70 Geburtstag Robert Schröder. 104 pages with 10 illustrations. Leipzig, Germany, 1955, Georg Thieme. DM 13.50.

This volume, in honor of Dr. Robert Schröder on the occasion of his seventieth birth-day, contains many articles by outstanding German gynecologists, pathologists, anatomists, and surgeons. The first two, by Dr. Hans Runge and Dr. Konrad Tietze, describe the life teachings and research of Dr. Schröder. The next fifteen articles cover both original research and published literature in the various fields of obstetrics and gynecology that interest Dr. Schröder. Exceptionally good articles were by H. Siebke, "Advances in Hormone Therapy in Gynecology," H. Lax and W. Mobius, "Genital Carcinoma," and G. Gaethgens, "Vitamin Therapy in Menstrual Disfunctions."

Atlas of General Surgery. By J. R. Wilder. 222 pages with 101 illustrations. St. Louis, 1955, The C. V. Mosby Company. \$13.50.

It should be pointed out that although this book includes many operations employed in general surgery, it does not include many employed in surgical specialties. The illustrations are quite accurate sketches, but often lack details important for proper execution of an operation. Sections devoted to surgery of the gastrointestinal tract are quite adequate and have most informative illustrations.

The section illustrating female pelvic surgery is very inadequate and inaccurate Probably it should have been omitted.

Biologische Daten für den Kinderarzt, Vol. I and Vol. II. By Joachim Brock. Second edition. 1834 pages with 255 illustrations. Berlin, Germany, 1955, Springer-Verlag. DM 125 and DM 73, respectively.

Although written primarily for pediatricians, this book contains much material interesting to obstetricians and gynecologists, i.e., that dealing with growth, development, and physiology of the newborn (both term and premature), and that dealing with physiological changes of puberty and menarche. The first volume is devoted to growth, body weight and length, skeletal system, blood and circulation, respiratory system, nutrition, digestion, and intestinal flora. The second volume deals with metabolism (chemical and physical), urinary system, endocrine secretions, nervous system, cerebrospinal fluid, electroencephalography, hypothalamus and autonomic nervous system, psychology, skin, bacterial defenses, and biometrics.

Most of the material on physiology is up to date, including the discussion of adrenocorticosteroids, cobalt, copper, and iron. The author states, however (pages 149-150, vol. II), that while hormones of the mother can participate in fetal metabolism, the obverse can occur and the fetal pancreas can supply insulin to the diabetic mother, accounting for the lack of change in insulin requirement in some diabetic mothers during pregnancy.

The bibliography is lengthy, based mainly on the German literature. Since each section is written by a different author, the style of writing and difficulty of construction vary, but should not pose any problem for American physicians who read German. Among the illustrations are interesting tables of values of growth and development, especially those of premature infants.

Since only parts of the book are of major interest to obstetricians and gynecologists, it is best recommended as a reference text. It is useful because it combines basic elements of biochemistry and physiology with special references to the fetus, infant, child, and adolescent, and makes important material easily available.

Gynecology. Vol. II, Surgical Techniques. By Robert J. Lowrie. 523 pages. Springfield, Ill., 1955, Charles C Thomas, Publisher. \$17.75.

This excellent reference book contains contributions of more than 60 specialists in the United States, Canada, and England. The subject matter is covered comprehensively; more than 65 independent operative procedures, including much original work, are described. Different procedures used to correct the same condition are described (e.g., 6 for correction of stress incontinence and 4 for repair of urinary fistula). The binding and paper are good; the type, legible; and the illustrations, profuse and of high caliber. Many illustrations have appeared previously in texts or in articles.

The material not related to surgical technique (e.g., religious and medicolegal aspects of sterilization; indication, incidence, and mortality in cesarean section) might well have been omitted.

This book is valuable because it makes readily available practically all techniques used in gynecological surgery.

Obstetrical Practice. By Alfred C. Beck and Alexander H. Rosenthal. Sixth edition. 1066 pages with 969 illustrations. Baltimore, 1955, Williams & Wilkins. \$12.00.

The sixth edition of Beck's Obstetrical Practice has been a pleasure to review. Although retired from practice, Dr. Beck continues to exhibit a scholarly and practical interest in obstetrics. Dr. Rosenthal, co-author, is a Clinical Associate Professor of Obstetrics and Gynecology, State University of New York, and former resident and associate of Dr. Beck. Dr. Rosenthal's additions are those of a person engaged in the daily practice of obstetrics and gynecology.

This book is well documented with important original contributions, both recent and old. Noteworthy is the documentation of new material concerning the physiology of pregnancy.

Advances in general medicine and the basic sciences which have affected the practice of obstetrics are included. In the management of pregnancy complicated by any

serious disease, it is stressed that treatment of the disease is the primary factor. Newer tools in the practice of medicine, such as availability of blood and antibiotics, have changed obstetrical concepts; for example, there are relatively few indications for extraperitoneal cesarean section, and version and difficult forceps operations. Furthermore, there is a reduced waiting period advised for manual removal of the placenta when the third stage of labor is prolonged. The newer work on hypofibrinogenemia is given in both its practical and theoretical aspects.

The chapter, "Diseases of the Decidua and Fetal Membranes," is not sufficiently comprehensive: it does not present the classic work of Hertig on this subject. Information about the "cardiac cripple" who is surgically rehabilitated for pregnancy is omitted. Effects of various analgesic and anesthetic agents on the blood oxygen saturation of the newborn are not included.

Students, teachers, and practitioners will find this a valuable text, and a worthy successor to other editions of Beck's book.

Understanding Surgery. Edited by Robert E. Rothenberg. 620 pages with 102 illustrations. New York, 1955. Pocket Books. \$.50.

This book helps fill a major gap in surgeon-patient relationships by providing information about many small things that bother the average patient a great deal, but about which he hesitates to ask the doctor lest he waste precious time. By providing this information, the author does much to relieve the patient of uneasiness and unrest.

The book is divided into sections corresponding to the various subspecialties and is profusely diagrammed. Although most of the language is understandable to the layman, occasionally the author assumes too much of the layman's medical background. The index in particular might confuse the lay reader.

The Hormones: Physiology, Chemistry and Applications. Vol. III. Edited by Gregory Pincus and Kenneth V. Thimann. 1012 pages. New York, 1955, Academic Press, Inc. \$22.00.

This excellent book not only supplements Volumes I and II, but in many respects supplants them. The chapters include reviews of plant growth hormones, hormones in invertebrates, neurohormones, physiology and chemistry of parathyroids, hormones of the Islets of Langerhans, anterior and posterior pituitary hormones, chemistry and physiology of the thyroid, chemistry and metabolism of steroid hormones, physiology of ovarian and testicular hormones, physiology of the adrenal cortex, and clinical endocrinology.

Selected Abstracts

New York State Journal of Medicine

Vol. 55, No. 8, April 15, 1955.

Hunter, Oscar B., Jr.: Cortisone in the Management of Hemolytic Disease in the Newborn, p. 1136.

Robertson, Theodore: The Use and Abuse of Blood Transfusions, p. 1140.

*Sawitsky, Arthur, and Plotkin, David: Hypofibrinogenemia and Postpartum Hemorrhage, p. 1153.

Gould, Irving D.: Rheumatoid Arthritis Aggravated by Pregnancy and Controlled by Cortisone, p. 1164.

Fitzgerald, James A., and Crossley, James L.: Clinical Vagaries of the Stein-Leventhal Ovary, p. 1179.

*Schaefer, George: Proceedings, Special Committee on Infant Mortality: Clinical Management of the Pregnant Woman With Tuberculosis, p. 1189.

Sawitsky and Plotkin: Hypofibrinogenemia and Postpartum Hemorrhage, p. 1153.

The physiology of coagulation defects associated with low fibrinogen levels is reviewed. Three tests useful clinically to determine hypofibrinogenemia are described. They are: (1) Tube test—5 c.c. of the patient's blood is incubated at 37° C. for 45 minutes. If no clot appears or if the clot disintegrates, the fibrinogen level is critically low. (2) Quantitative blood fibrinogen determination—this is too cumbersome for emergency use. (3) Schneider fibrin titer assay—the blood in question is successively diluted in a series of 8 tubes. The resultant dilutions of the plasma component are 1, 10, 50, 100, 200, 400, 800, 1,600. Topical thrombin is then added and coagulation should occur in one minute. A fibrin titer above 400 is usually normal. Sixteen successfully treated cases of postpartum hemorrhage associated with coagulation defects are reported. In most instances from 2 to 6 Gm. of fibrinogen were necessary for rapid restoration of the blood level. If fibrinogen cannot be obtained, the authors note that each 500 c.c. of whole blood contains approximately 500 mg. of this plasma fraction. Conditions in which fibrinogenopenia may occur are listed.

STEWART A. FISH, M.D.

Schaefer: Clinical Management of the Pregnant Woman With Tuberculosis, p. 1189.

The importance of early diagnosis of pulmonary tuberculosis by routine chest x-ray is pointed out by Schaefer. When tuberculosis and pregnancy are associated, the question arises as to the effect of pregnancy on the disease and vice versa. From this study it seems obvious that pregnancy does not necessarily have a deleterious effect upon pulmonary tuberculosis, either active or inactive. Medical treatment during pregnancy consists of bed rest and the usual supportive measures. Pneumothorax is not contraindicated nor is thoracoplasty. Pneumoperitoneum immediately after delivery, in an attempt to maintain the intra-abdominal pressure at pregnancy levels, is apparently of no practical value. Lung resection has become a recent adjunct in the treatment of localized disease and the author reports one case of normal pregnancy and delivery after lobectomy performed during the second month of gestation. Streptomycin, para-aminosalicylic acid, and isoniazid are the major adjuvants in the medical treatment of tuberculosis in pregnancy. There is no evidence that any of these drugs affects the fetus in utero adversely. Delivery

should be conducted with very little analgesia and preferably conduction anesthesia, in order to prevent dissemination of the pulmonary disease during general anesthesia. The author points out that therapeutic abortion is rarely indicated in pulmonary tuberculosis. None of the infants of this series was born with tuberculosis and the rarity of congenital tuberculosis is emphasized. Isolation of the newborn from the mother is mandatory if there is evidence of active disease. The problem of B.C.G. vaccination and socioeconomic factors are discussed, and it is noted that repeat pregnancies are not necessarily contraindicated in women with arrested disease.

STEWART A. FISH, M.D.

Vol. 55, No. 10, May 15, 1955.

Gruhn, John G.: The Transfusion of Blood, Components, Plasma, and Extenders, p. 1441.

Vol. 55, No. 11, June 1, 1955.

Smessaert, Andre, Collins, Vincent J., and Kracum, Vincent D.: Aerosol Administration of Alevaire II, p. 1587.

Adlerman, Edwin J.: Urologic Origins of Backache, p. 1598.

Jacobsen, Victor C.: Premenstrual Edema and Related Problems, p. 1610.

Gerhardt, Paul R., and Handy, Vincent H.: Factors Related to Cancer Treatment, p. 1634.

Vol. 55, No. 16, August 15, 1955.

Greene, H. J., and Pomerance, William: Carcinoma of the Vulva, p. 2353.

Wiener klinische Wochenschrift

Vol. 67, No. 1, January 7, 1955.

Antoine, T.: Hormone Therapy in Carcinoma of the Female Genital Tract, p. 14.

Vol. 67, No. 3, January 21, 1955.

Bruecke, F.: The Effect of Hormones on Malignant Tumors, p. 45.

Reitinger, J., and Riess, H.: Prophylaxis and Treatment of Thrombosis in Pregnancy and Confinement, p. 56.

Vol. 67, No. 4, January 28, 1955.

Thalhammer, O.: Four Examples of Congenital Disease, p. 68.

Vol. 67, No. 6, February 11, 1955.

Zacherl, H.: The Gynecologist's Point of View on Therapeutic Abortion, p. 103.

Vol. 67, No. 7, February 18, 1955.

Mlczoch, F.: Drug Therapy for Hypertension, p. 117.

Husslein, H.: Nutrition and Pregnancy, p. 129.

Vol. 67, No. 9, March 4, 1955.

Tapfer, S.: Symptomatology and Treatment of Pre-eclampsia and Eclampsia, p. 153.

Vol. 67, No. 10, March 11, 1955.

Fleischhacker, H.: Symptomatic Treatment in Cancer, p. 169.

*Koelbl, H.: Immediate and Ultimate Results in Erythroblastosis Fetalis After Exchange Transfusion, p. 172.

Kofler, E., and Palmrich, A. H.: Influence of Follicle Hormone on the Origin and Growth of Carcinoma of the Fundus, p. 176.

Koelbl: Immediate and Ultimate Results in Erythroblastosis Fetalis After Exchange Transfusion, p. 172.

One hundred and sixty-eight cases are reported. Treatment falls into three groups: (1) blood transfusion; (2) exchange transfusion several hours after delivery; and (3) immediate exchange transfusion. The respective mortality rates of 50 per cent, 12.5 per cent,

and 5.4 per cent emphasize the obvious importance of haste in the treatment of these children. Even at best, the fetal mortality is high, because these babies are particularly vulnerable to birth trauma and neonatal disease. In view of the tendency toward infection, it is suggested that prophylactic antibiotics can improve the results.

WALTER F. TAUBER, M.D.

Vol. 67, No. 11, March 18, 1955.

Feurstein, V.: Homologous Serum Jaundice and Blood Transfusions, p. 193.

Vol. 67, No. 12, March 25, 1955.

Hienert, G.: Cardiac Arrest, p. 203.

Vol. 67, No. 17, April 29, 1955.

Kratochvil, K.: Early Diagnosis and Treatment of Carcinoma of the Breast, p. 297.

Vol. 67, No. 18, May 6, 1955.

Rigler, R., and Rosenkranz, W.: On the Mechanism of Deciduoma Formation, p. 316.

Just, O., and Linder, F.: The Importance of Controlled Hypotension in Surgery, p. 318.

Vol. 67, No. 22, June 3, 1955.

*Hüber, E. F., and Thaler, H.: The Heart and Pregnancy, p. 389.

Hüber and Thaler: The Heart and Pregnancy, p. 389.

Pregnancy increases the load on the heart, but in most cases there is a sufficient reserve to cope with this. Four per cent of pregnant women have circulatory symptoms; half of these have organic heart disease; and 75 per cent of these have rheumatic heart disease. In general, the prognosis is influenced by the cardiac reserve and the degree of compensation. In mitral stenosis, however, pressure in the pulmonary artery, which can be determined only by cardiac catheterization, is the determining factor. In evaluating compensation, it must be borne in mind that a certain degree of dyspnea appears also in normal pregnant women. The prognosis of the Class I cardiac patient varies but little from the normal, if she is properly supervised, her weight well controlled, and her sodium intake limited. Mortality among Class III and IV cardiac patients, however, is 5 per cent and 20 per cent, respectively, with accompanying poor prognosis for the baby. The periods of greatest danger are in the sixth to the eighth lunar months, during labor, and in the immediate puerperium. There is also a sharp increase in risk beyond the age of 35.

In advising women with heart disease on contemplated pregnancies, the main medical factors to be considered are the degree of compensation and the patient's age. In multiparas, the ease or difficulty with which previous pregnancies were tolerated furnishes a good lead. Parity may be taken into consideration in the interest of avoiding an only child, if the patient withstood her previous pregnancy without undue difficulty.

Interruption of pregnancy should be considered in cases where the vital capacity decreases sharply, pulmonary artery pressure rises, an episode of heart failure has been previously observed or determined from the history, or auricular fibrillation is present. Auricular fibrillation offers an especially poor prognosis. Interruption in cases where it appears desirable to terminate the pregnancy is relatively easy in the first trimester, when abortion can be effected relatively safely by curettage. In more advanced pregnancies, the danger of hysterotomy must be weighed against that of permitting the pregnancy to continue. Usually laparotomy is more hazardous than a well-supervised prenatal course, provided only that the patient is cooperative and facilities are available for proper care.

Pregnant cardiac patients should be protected against subacute bacterial endocarditis by the prophylactic use of penicillin and streptomycin. The second stage of labor should be shortened by the use of low forceps. The anesthesia of choice for delivery, or for any

surgical intervention that may become necessary, is ether which permits maintenance of high oxygen levels. Heart disease, per se, is no indication for cesarean section which should be done only for possible intercurrent obstetrical reasons.

WALTER F. TAUBER, M.D.

Wiener medizinische Wochenschrift

Vol. 105, No. 1, January 8, 1955.

*Heidler, H.: Etiology and Treatment of Gynecological Bleeding, p. 1.

Tapfer, S.: Menopausal Symptoms and Their Treatment, p. 24.

Heidler: Etiology and Treatment of Gynecological Bleeding, p. 1.

The physiology of the menstrual cycle in terms of pituitary, ovary, and endometrium is reviewed. Metrorrhagia due to malfunction at any one point in this scheme, carcinoma of the uterus and cervix, and cervical polyps are discussed. Treatments suggested include dilatation and curettage, the use of ergot preparations and Pitocin, for the benign conditions. It is also advised that androgens, estrogens, and progesterone be used in selected cases. If irregular bleeding, proved to be of benign origin, occurs close to the menopause, the author suggests that x-ray castration may be indicated. Bleeding due to benign erosions and vaginitis is treated with bacteriostatic agents. When the bleeding is due to functional ovarian tumors or fibroids, laparotomy must be performed.

WALTER F. TAUBER, M.D.

Vol. 105, No. 3, January 22, 1955.

*Reitinger, J.: Cesarean Sections With Special Consideration of Increasing Indication, p. 57.

Reitinger: Cesarean Section With Special Consideration of Increased Indication, p. 57.

The cesarean sections of Division II, Department of Gynecology, University of Vienna, between 1942 and 1952 are summarized. The section rate is 1.04 per cent with a corrected maternal mortality of 1.53 per cent and a fetal mortality of 4.21 per cent. The indications for sections recognized are: cephalopelvic disproportion, placenta previa, toxemia of pregnancy, elderly primiparity, postmaturity, uterine inertia, and malposition. The last four mentioned of these represent a recent extension of indications for this procedure. In partial placenta previa, version and breech extraction with a Willett forceps to the vertex, after artificial rupture of the membranes, are employed.

Except when hysterectomy is associated with the procedure, low cervical transverse section is almost always used. The exceptions cited included sections undertaken with (1) carcinoma of the cervix, (2) fibromyomas of the uterus, and (3) previous multiple sections.

The anesthesia of choice is nitrous oxide and curare.

WALTER F. TAUBER, M.D.

Vol. 105, No. 8, February 26, 1955.

Kalkschmid, W.: The Ability to Breastfeed in Patients Receiving Estrogens as Oxytocics, p. 151.

Vol. 105, No. 9, March 5, 1955.

Koenig, W.: Physical Therapy in Functional Disturbances in Gynecology, p. 167.

Zeitschrift für Geburtshilfe und Gynäkologie

Vol. 143, No. 1, 1955.

Sander, M.: The Placenta, an Active Defense Organ of the Fetus in Heterospecific Pregnancy, p. 1.

*Trap, J.: Mechanism of Delivery in Breech Presentation, p. 30.

- *Sas, M., and Rapscak, W.: Studies of Excretion of Neutral 17-Ketosteroids in Gynecological Disease and During Gestation, p. 40.
- Meissert, H. W.: Thrombin Inhibitors and Antithrombin in the Newborn, p. 54.
- Mosler, W.: Malformations in Relation to the Rh Factor, p. 61.
- *Bleier, W.: Gartner's Duct Cysts of the Vagina Coupled With Other Maldevelopments of the Urogenital System, p. 71.
- Winter, G. F.: Variations of the Endometrium, p. 86.

Trap: Mechanism of Delivery in Breech Presentation, p. 30.

The author shows statistically that, in a large series of breech presentations, the best results, as far as fetal mortality is concerned, occur when the delivery is allowed to continue spontaneously and without help from the obstetrician. In a series of cases it was demonstrated that no death occurred when the labor was allowed to continue alone; there was an 8.2 per cent primary mortality with some manual help; and a 38.2 per cent mortality when extraction of the baby was done. The methods of Bracht of Germany and Covjanov of Russia are described. Both depend on the absence of cephalopelvic disproportion. In essence these methods consist of allowing the labor to continue until dilatation of the cervix is complete. The membranes are allowed to remain intact. Vaginal examination is done only at this time to rupture the amniotic sac and determine the exact stage of dilatation and verify the absence of a prolapsed cord. Delivery is allowed to continue without interference until the anterior scapula has presented and rotated either to the oblique or the transverse. At this time the fetal trunk and pelvis are supported and elevated, and the head allowed to be delivered spontaneously.

In conclusion, the author states that the best procedure of delivery in breech position utilizes the forces of the uterine and abdominal musculature, rather than obstetrical interference. Manual help is not only superfluous but harmful, even with larger babies. The mechanism of breech delivery is disturbed only by premature obstetrical activity, and best results are obtained with natural forces only.

L. B. WINKELSTEIN, M.D.

Sas and Rapcsak: Studies of Excretion of Neutral 17-Ketosteroids in Gynecological Disease and During Gestation, p. 40.

Excreted neutral 17-ketosteroids are minimal in childhood in both sexes. In the female, excretion begins at puberty and increases until the late thirties. From the fortieth year excretion begins to decrease. The average values at all ages range between 10 and 14 mg. per 24 hour urine specimen as calculated by the Zimmerman method.

Studies of excretion of neutral 17-ketosteroids at various ages and in different pathological and physiological conditions were made. In the female there was no variation in excretion with the changes in the menstrual cycle or with menstruation. In cases where ovarian functional changes were suspected (uterine displacement, adnexitis, endometritis, fibromyomas of the uterus, benign ovarian cysts, genital tuberculosis, hyperestrinism, ovarian amenorrhea, pituitary amenorrhea, and genital cancer) no changes were noted. The author states from his observations that, under normal conditions, the ovary has no part in the production of 17-ketosteroids. Even with bilateral oophorectomy secretion is not reduced. During gestation, excretion corresponds to the higher values of the nonpregnant female. Before delivery the total excretion is increased. On the day preceding labor, however, a marked decrease was observed. During the puerperium there are moderate decreases; the lowest values are reached on the third postpartum day. After this, increases occur till normal values are reached. A similar curve is noted with spontaneous abortion. When postmaturity occurred, values corresponded to those found in normal pregnancy. In toxemia of pregnancy, no uniform or constant excretory results were obtained,

L. B. WINKELSTEIN, M.D.

Bleier: Gartner's Duct Cysts of the Vagina Coupled With Other Maldevelopments of the Urogenital System, $p.\ 71$.

Three cases of Gartner's duct cysts were described, together with a review of six cases culled from the world literature. In two of the three cases, the cysts communicated with the vagina through a canal in the cervix. In the third the cyst was closed. All cysts were infected. All cases were of interest because they were accompanied by malformations of the urogenital system. In one, aplasia of the kidney was noted; in the second, congenital dilatation of the ureter; in the third, kidney and ureteral duplication were present bilaterally. This last patient also had a duplex uterus and a cardiac ventricular septal defect.

The importance of a thorough study of both the urinary and genital systems is stressed in all cases where the diagnosis of Gartner's duct cyst is made. Retroperitoneal pneumograms, hysterosalpingography, and arteriography are only some of the special procedures to be employed.

L. B. WINKELSTEIN, M.D.

Journal of Clinical Endocrinology and Metabolism

Vol. 15, No. 9, September, 1955.

*Payne, H. W., and Latour, J. P. A.: Quantitative Estimations of Endometrial Glycogen, Using the Anthrone Method, p. 1106.

Payne and Latour: Quantitative Estimations of Endometrial Glycogen, Using the Anthrone Method, p. 1106.

Glycogen is believed by many to be the direct source of nutriment for the early conceptus from the time it enters the uterine cavity to the time it is actively supported by the maternal blood stream. Much work has been done to correlate abnormalities of glycogen deposition with primary sterility.

The authors obtained specimens of endometrium from uteri removed by hysterectomy and by endometrial biopsy. They then submitted these endometrial specimens to a quantitative determination for glycogen.

Their results indicate that glycogen is low or absent in the proliferative endometrium. It is present in appreciable amounts in secretory endometrium but the amount varies during the secretory phase. It is highest on day 17 and lowest on days 21 to 22.

J. EDWARD HALL, M.D.

The Lancet

Vol. 1, June 11, 1955.

*Jeffcoate, T. N. A., and Wilson, J. K.: The Effect of Hydergine on Uterine Action, p. 1187.

Jeffcoate and Wilson: Effect of Hydergine on Uterine Action, p. 1187.

Hydrogenation of the alkaloids of ergot has been reported to deprive them of their oxytocic and vasoconstrictor properties and endow them with spasmolytic ones (Stoll, A.: Indian J. Pharm. 15: 200, 1953). In this study Hydergine, which contains the dihydroderivatives of ergocornine, ergocryptine, and ergocristine in equal proportions, was employed. At the time of labor, 0.6 mg. of the drug in 1 L. of 5 per cent dextrose was given intravenously to 5 primigravidas. Three patients noted no change in the site and intensity of the labor pains. Two noted an increase and in these and one other instance tocographic records suggested that the drug had an oxytocic effect. In only one instance was reduction in uterine activity suggested. Of 109 primigravidas in normal labor at term, 59 received 0.15 mg. of Hydergine intramuscularly at hourly intervals for 4 doses and 50 acted

as controls. All patients received 1/4 grain of morphine and 0.1 gram pethidine when the cervix was 2 to 3 fingers dilated. No significant difference was noted in the length of the first and second stages of labor and the course of the third stage was almost identical. In 17 women with inefficient uterine action the results were equivocal. If the drug did quicken some of the labors oxytocic action is suggested as being more likely than reduction of hypertonus. In only 2 instances did a quieting and regulating effect on uterine behavior appear to occur. In 4 women who were receiving an oxytocic drip infusion for the purpose of inducing labor, the drug may have increased the frequency and strength of the contractions in two. In the third patient the effect of oxytocin was accentuated when Hydergine was given at a rate of 90 drops a minute but the contractions became less intense without change in frequency when the infusion rate was increased. In the fourth case the contractions were less intense after the drug was given. A possible inhibitory action of Hydergine is suggested by the tendency to uterine relaxation and hemorrhage during and after the third stage but this effect may also be explained by the withdrawal of the oxytocic action when the drug was discontinued at the time of full cervical dilatation. The conclusion is reached that despite laboratory evidence hydrogenation of the ergot alkaloids does not deprive them of their oxytocic action, even less reverses it. The use of these compounds involves a risk not compensated by any demonstrable effect on uterine efficiency.

DAVID M. KYDD, M.D.

Vol. 2, July 9, 1955.

*Moore, Keith L., and Barr, Murray L.: Smears From the Oral Mucosa in the Detection of Chromosomal Sex, p. 57.

Cummin, R. C.: Cervical Pregnancy, p. 68.

Tomkinson, J. S.: Tissue-Forceps for Cesarean Section, p. 71.

Moore and Barr: Smears From the Oral Mucosa in Detection of Chromosomal Sex, p. 57.

In 140 instances (81 males and 59 females), the characteristic female sex chromatin was visible in the nuclei of epithelial cells obtained from the oral mucosa of females while a similar chromatin mass was not seen in cells obtained from the oral mucosa of males. Such a determination is simpler than skin biopsy for the detection of chromosomal sex in congenital errors of sex development.

DAVID M. KYDD, M.D.

Vol. 2, July 16, 1955.

St. Van Eps, L. W.: Psychoprophylaxis in Labor, p. 112.

*Carpentier, P. J., and Janssen, P. A.: a-p-Methoxy-phenyl a-Di-n-Butylaminoacetamide in Dysmenorrhea, p. 122.

Carpentier and Janssen: a-p-Methoxy-phenyl a-Di-n-Butylamino-acetamide (A.16) in Dysmenorrhea, p. 122.

Either 50 mg. A.16 (Janssen, P. A.: J. Am. Chem. Soc. 76: 6192, 1954; de Jongh, D. K., Janssen, P. A., and van Proosdij-Hartzema, E. G.: Acta physiol. pharm. neerl. 3: 331, 1954) or a placebo was given to female volunteers who had had dysmenorrhea for several years at every period. Neither the patient nor the physician knew whether the patient received the drug or a placebo. Tabulation of the results showed a strikingly high number of good results following the administration of the placebo (48 per cent). Nonetheless, A.16 caused a significantly greater number of good results (68 per cent). No side effects were noted.

DAVID M. KYDD, M.D.

Vol. 2, July 23, 1955.

*Kelsall, G. A., and Vos, G. H.: Premature Induction of Labor in the Treatment of Hemolytic Disease of the Newborn, p. 161.

Rountree, P.: Streptococcus Pyogenes Infections in a Hospital, p. 172.

Kelsall and Vos: Premature Induction of Labor in the Treatment of Hemolytic Disease of the Newborn, p. 161.

In a series of 246 consecutive incompatible pregnancies in mothers whose sera contained abnormal rhesus antibodies against their infants, the pregnancy terminated spontaneously in 130 instances and the labor was induced prematurely in 116. In the first group, 36 of the progeny were stillborn and 9 died shortly after birth (total mortality of 34.6 per cent). In the second, 3 infants were stillborn and 12 died after birth (mortality 12.9 per cent). These figures include deaths from all causes including 3 deaths and one live baby in pregnancies ended by induction before the thirty-fifth week of gestation and 19 deaths in pregnancies that ended spontaneously before the thirty-fifth week. By eliminating these early terminations the authors "compare" their series with the one reported by Mollison and Walker (Lancet 1: 261, 1952). The cases of induced labor in the present series had an infant mortality of 10.7 per cent (100 infants survived, 11 died after birth, and 1 was stillborn). The cases which were allowed to terminate spontaneously had a mortality of 23.4 per cent (85 infants survived, 7 died after birth, and 26 were stillborn). These results differ strikingly from those of Mollison and Walker who found the mortality in the induced termination of pregnancy to be 36.4 per cent and in the spontaneous to be 24.1 per cent. The two series are not strictly comparable because the present authors terminate by induction all such pregnancies when they demonstrate an appreciable and particularly a rising titer of antibodies in the mother's serum. Only those cases over which they had no control were allowed to proceed to a spontaneous delivery. By happenstance the series contains approximately equal numbers. The authors believe that careful and repeated determinations of the antibodies in the mother's serum allow them to leave the fetus in utero for as long as possible consistent with a harmless antibody titer. As soon as birth occurs, an exchange transfusion is undertaken with 150 to 250 ml. of Rh-negative blood per pound of body weight of the infant. Heparin rather than citrate is used as an anticoagulant because of the danger of hypocalcemic tetany when the latter chemical is used. Fresh blood rather than stored blood lessens the risk of potassium intoxication. Blood that has been acquired from male donors is used. If some female blood must be used, it is used during the early part of the exchange transfusion in order that male blood may be left in the infant.

In this series, premature induction of labor at the optimal time after 35 weeks of gestation associated with exchange transfusion of the infant largely eliminated stillbirths without increasing the number of neonatal deaths.

DAVID M. KYDD, M.D.

Vol. 2, August 13, 1955.

*Penrose, L. S.: Parental Age and Mutation, p. 312.

Russell, J. K.: Lower-Segment Cesarean Section for Placenta Previa, p. 322.

O'Dwyer, J. P.: Rupture of the Lower-Segment Cesarean-Section Scar, p. 324.

Penrose: Parental Age and Mutation, p. 312.

Spontaneous mutation in a cell in the germ line might be due to various causes of which the most obvious are: (1) failure to copy the genes correctly at cell division, (2) irradiation from natural sources, and (3) chemical mutagenic agents. In the first, the father's age is of more significance than the mother's inasmuch as the spermatogonia are continually dividing. In the second, both sexes might be affected equally irrespective of the number of cell divisions. In the third, if the mutagenic agent is a chemical (such as a toxic by-product of normal metabolism suggested by Haldane) that accumulates in the germ cells, the ova would be more affected than the sperm. This effect would be more marked in the case of a multiplying agent such as a virus. In the third, then, the age of the mother would have a greater influence than the age of the father. These considerations make the difference between mean ages of fathers and mothers for a particular condition a sensitive and critical measurement. Using data obtained from the literature a

number of conditions are examined. In Mongolism and dizygotic twinning the mother's age is dominant. In achondroplasia the father's age is significant and argues that this condition is due to a mutation having to do with a copying failure. In other congenital defects such as acrocephaly, anencephaly, and hydrocephaly the relationship is less clear. The observation that for constant maternal age groups the father's age was significantly associated with the general stillbirth rate even though the influence of the father was weaker than that of the mother suggests that fresh mutations not uncommonly cause mortality in early life. These inconclusive data are cited to emphasize the need for a comprehensive inquiry.

DAVID M. KYDD, M.D.

Vol. 2, September 3, 1955.

*Dennison, W. M.: Hematogenous Osteitis in the Newborn, p. 474.

*O'Sullivan, D. J., Higgins, P. G., and Wilkinson, J. F.: Oral Iron Compounds, p. 482.

Dennison: Hematogenous Osteitis in the Newborn, p. 474.

Of 41 cases of osteitis seen during the neonatal period, 22 were considered to be benign in the sense that at no time did the infant's life appear to be in danger although 6 of these children were left with permanent deformities due to bony destruction in the head of the humerus (3 cases), head of the femur (2 cases), and in the distal epiphysis of the femur (1 case). In the 19 severe cases, there were 4 deaths and recurring infection, sequestrum formation, and epiphyseal and metaphyseal damage led to a high morbidity although no detailed analysis of the final result in this group is given. Instead, 5 so-called typical case histories are given in some detail. In these 19 seriously ill infants the infection was caused by an anaerobic streptococcus in one fatal case and in one case the offending organism was not isolated. The remaining 17 infections were caused by a coagulase-positive Staphylococcus aureus which was sensitive to penicillin in two instances, resistant in 14, and the sensitivity was not assessed in one instance.

The observation that minor staphylococcus infections appear in 10 to 15 per cent of infants and the incidence is increasing (Capon, N. B.: Brit. M. J. 1: 803, 1955) is stressed. Also, the fact that the septicemia had presented as pneumonia or as gastroenteritis and only the appearance of a swollen limb or joint caused the correct diagnosis to be made emphasizes the importance of immediate and adequate therapy of these conditions and also the importance of realizing the possibility that the infant may have septicemia. The use of penicillin and streptomycin is recommended in preference to long-continued use of chlortetracycline.

DAVID M. KYDD, M.D.

O'Sullivan, Higgins, and Wilkinson: Oral Iron Compounds, p. 482.

Ferric hydroxide, ferrous sulphate, ferrous succinate, and ferrous gluconate in doses of 210 mg. of elemental iron were given to 80 patients. Ferric hydroxide in such doses was not effective but the other three compounds were equally efficacious. Patients refractory to one drug were refractory to all oral iron drugs. Intolerance appeared in 13 per cent of the patients taking ferrous sulfate and in 4 per cent of those taking the succinate or gluconate.

DAVID M. KYDD, M.D.

Vol. 2, September 10, 1955.

Labrum, A. H.: Ergometrine With Hyaluronidase, p. 522.

Correspondence

Possible Physiological Effects of X-ray Contrast Medium

To the Editors:

A recent experience with a new radiopaque medium for hysterosalpingography prompts this note concerning the possible physiological effects of this x-ray contrast substance.

A patient with a history of habitual abortion received a dose of 10 c.c. of Salpix (Ortho Pharmaceutical Corporation) on Aug. 4, 1955.

Six months later the protein-bound iodine remains over 25 mcg. per cent on repeated determinations and the I¹³¹ uptake is in the myxedematous range. The patient does not have clinical evidence of hypothyroidism but it would obviously not be to her advantage to be thyroid deficient since she is again apparently pregnant. Desiccated-thyroid therapy has therefore been instituted.

Although there is not clear-cut evidence of thyroid depression from such exogenous organic iodine compounds, the possibility should be kept in mind that the diagnostic use of Salpix may result in laboratory evidence of thyroid suppression. It may constitute another reason for the administration of thyroid substance in pregnancy in the otherwise euthyroid individual.

B. J. DUFFY, JR., M.D. DIRECTOR, ISOTOPE LABORATORY

GEORGETOWN UNIVERSITY HOSPITAL WASHINGTON 7, D. C. MARCH 2, 1956

Reply

To the Editors:

One of our recent clinical studies has just come to my attention. This study was conducted on routine infertility cases. Some were euthyroid and some were hypothyroid. All were examined by hysterosalpingography using Salpix. If thyroid was indicated, they received it. Of 33 such patients, over 60 per cent became pregnant within six months following hysterosalpingography, and all who became pregnant were delivered of normal, healthy infants. With such random sampling, this evidence appears to contradict the findings in Dr. Duffy's single case.

Dr. Duffy's patient in question had a history of habitual abortion. This could indicate that an endocrine imbalance might exist as a possible cause of her difficulty without clinical symptoms. Certainly a thyroid activity study would be indicated as well as a hysterosalpingogram. She should be treated according to all the laboratory and clinical findings.

I find in my letter to Dr. Duffy a typographical error on the amount of iodide in Lugol's solution. It should read 0.225 to 0.3 Gm. of iodide per day over periods of two to four weeks. The iodide concentration in Salpix and other organic iodine diagnostic media varies from 0.3485 Gm. of iodide per cubic centimeter for Salpix to as much as 0.52 Gm. of iodide per cubic centimeter in others. In Dr. Duffy's case, 3.485 Gm. of iodide in Salpix as a single dose was introduced intravaginally one time only. Other diagnostic iodide preparations are given in amounts of 1 Gm. to 13.9 Gm. of iodide intravenously without, to the best of my knowledge, any permanent endocrine imbalances.

ORTHO PHARMACEUTICAL CORPORATION W. THOMAS SPAIN, M.D.,
DIRECTOR OF MEDICAL SERVICE.

RARITAN, N. J. APRIL 10, 1956.

Items

American Board of Obstetrics and Gynecology

Applications for certification (American Board of Obstetrics and Gynecology) for the 1957 Part I Examinations are now being accepted. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of applications is Oct. 1, 1956.

All candidates for admission to the Examinations are required to submit with their application a plain typewritten list of all patients admitted to the hospitals where they practice, for the year preceding their application or the year prior to their request for reopening of their application.

Application for re-examination, as well as requests for resubmission of case abstracts, must also be made to the Secretary prior to Oct. 1, 1956.

Current Bulletins outlining present requirements may be obtained by writing to the Secretary's office.

ROBERT L. FAULKNER, M.D., SECRETARY AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY 2105 ADELBERT ROAD CLEVELAND 6, OHIO

John Harris Memorial Lecture Fund

A fund to provide for an annual lecture at the University of Wisconsin in the field of obstetrics and gynecology by some nationally known specialist has been established in memory of John Harris, late professor and head of the Department of Obstetrics and Gynecology at the University.

Contributions to the fund may be sent to Dr. John Z. Bowers, Dean, University of Wisconsin Medical School.

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January and July)

American Academy of Obstetrics and Gynecology. (1945) President, Ralph E. Campbell. Secretary, C. Paul Hodgkinson, 17546 Meadowood Ave., Birmingham, Mich. Next meeting, Palmer House, Chicago, Ill., Nov. 7-9, 1956.
 American Gynecological Society. (1876) President, Norman F. Miller. Secretary, Andrew A. Marchetti, Georgetown University Hospital, Washington 7, D. C.
 American Association of Obstetricians and Gynecologists. (1888) President, Lawrence M. Randall. Secretary, Frank R. Lock, Bowman Gray School of Medicine, Winston-Salem, N. C. Spring meeting, March 23 and 24, 1956. Annual meeting Sept. 6-8, 1956.
 Central Association of Obstetricians and Gynecologists. (1929) President. Harold L. Gainey.

Central Association of Obstetricians and Gynécologists. (1929) President, Harold L. Gainey. Secretary, Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Ill. Annual meeting, Roosevelt Hotel, New Orleans, La., Oct. 4, 5, and 6, 1956.

South Atlantic Association of Obstetricians and Gynecologists. (1938) President, John C.

Burwell, Jr., Greensboro, N. C. Secretary, Charles H. Mauzy, Bowman Gray School of Medicine, Winston-Salem, N. C. Next meeting, Francis Marion Hotel, Charleston, S. C., Feb. 6-9, 1957. Feb. 6-9, 1957.

A. M. A. Section on Obstetrics and Gynecology. Chairman, Frank R. Lock. Secretary, D. Frank Kaltreider, University Hospital, Baltimore 1, Md. Meetings with annual

A.M.A. meetings.

Society of Obstetricians and Gynaecologists of Canada. (1944) President, Brian D. Best, Winnipeg, Manitoba. Secretary, F. P. McInnis, 280 Bloor St. W., Toronto, Ont.

American Board of Obstetrics and Gynecology. (1930) President, Bayard Carter. Secretary, Robert L. Faulkner, 2105 Adelbert, Rd., Cleveland 6, Ohio.

Akron Obstetrical and Gynecological Society. (1946) President, Leon Moldavsky. Secretary, Carl J. Paternite, 159 S. Main St., Akron, Ohio. Meetings, quarterly.

Alabama Association of Obstetricians and Gynecologists. (1940) President, Buford Word, Birmingham, Ala. Secretary, Julian P. Hardy, 920 S. 19th St., Birmingham, Ala.

Alameda County Gynecological Society. (1951) President, Victor Koerper. Secretary, Wallace Lawson, 2975 Telegraph Ave., Berkeley 5, Calif. Meetings, fourth Wednesday of graph month overat June Laly Averets and December.

each month except June, July, August, and December.

Arkansas Obstetrical and Gynecological Society. (1953) President, John Walter Jones.

Secretary, Robert W. Ross, 908 Donaghey Bldg., Little Rock, Ark. Meetings, April and

Atlanta Obstetrical and Gynecological Society. (1954) President, Charles B. Upshaw. Secretary, George A. Williams, Suite 6, 710 Peachtree St., N. E., Atlanta 8, Ga. Meetings quarterly.

ings quarterly.

Birmingham Obstetrical and Gynecological Society. (1949) President, Hunter Brown.

Secretary, Clay N. Wells, 1714 11th Ave. S., Birmingham 5, Ala. Meetings, September,
December, February, and April.

Boston, Obstetrical Society of. (1861) President, Christopher J. Duncan. Secretary, A.

Gordon Gauld, 1180 Beacon St., Brookline 46, Mass. Meetings, January, February,
March, April, October, and November.

Bronx Gynecological and Obstetrical Society. (1924) President, Sol S. Schiffrin. Secretary,
Bernard Lapan, 1882 Grand Concourse, Bronx 57, N. Y. Meetings, fourth Monday,
October through April, inclusive.

Brooklyn Gynecological Society. (1890) President, William Pomerance. Secretary, Leslie

Brooklyn Gynecological Society. (1890) President, William Pomerance. Secretary, Leslie H. Tisdall, 615 Third St., Brooklyn 15, N. Y. Meetings, third Wednesday, October, November, January, February, March, April, and May.

Buffalo Obstetrical and Gynecological Society. (1946) President, Robert E. O'Connor. Secretary, Chester Kaminski, 333 Linwood Ave., Buffalo, N. Y. Meetings, first Tuesday, October through May.

October through May.

^{*}Changes, omissions, and corrections should be sent to the publisher, The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Mo. The number after the Society's name is the year of founding. For further information, address the respective secretaries.

Central New York Association of Gynecologists and Obstetricians. (1938) President,

Charles Gwynn. Secretary, William Redfield, 1502 State Tower Bldg., Syracuse 2, N. Y. Meetings, second Tuesday, January, March, May, September, and November.

Chicago Gynecological Society. (1878) President, Ronald R. Greene. Secretary, Clyde J. Geiger, 4753 Broadway, Chicago 40, Ill. Meetings, third Friday, October through June.

Cincinnati Obstetrical and Gynecological Society. (1876) President, John G. Fleming. Secretary, Edward Alberts. Meetings, third Thursday, September through May.

Cleveland Society of Obstetrics and Gynecology. (1947) President, Ralph Dial. Secretary, Righard Glove, 20119, Van Aken Blyd, Sheker Heights, 22, Ohio, Meetings, fourth

tary, Richard Glove, 20119 Van Aken Blvd., Shaker Heights 22, Ohio. Meetings, fourth Monday, September, November, January, March, and May.

Columbus Obstetric-Gynecologic Society. (1944) President, James B. Patterson. Secretary, Harry E. Ezell, 188 E. State St., Columbus, Ohio. Meetings, last Wednesday of month, September through May, except December.

Dallas-Fort Worth Obstetrical and Gynecological Society. (1948) President, D. G. Harrell.

Secretary, H. I. Kantor, 3534 Maple Ave., Dallas, Texas. Meetings, spring and fall.

Dayton Obstetrical and Gynecological Society. (1937) President, E. E. Pinnell. Secretary,
J. C. Burt, 1130 Fidelity Bldg., Dayton, Ohio. Meetings, third Wednesday, September through May.

Denver Gynecological and Obstetrical Society. (1942) President, Paul Isbel. Secretary, Charles R. Freed, 1809 E. 18th Ave., Denver 18, Colo. Meetings, first Monday of every month, October through May, inclusive, unless otherwise notified.

El Paso County Obstetrical and Gynecological Society. (1948) President, Erich Spier.

Secretary, Alvin L. Perry, 209 Medical Arts Bldg., El Paso, Texas. Meetings, last
Thursday, every other month.

Florida Obstetric and Gynecologic Society. (1948) President, J. Champneys Taylor. Secretary, R. B. Chrisman, Jr., 356 Alhambra Circle, Coral Gables 34, Fla.

Georgia State Obstetrical and Gynecological Society. (1951) President, Hartwell Boyd. Secretary, J. Lon King, Jr., 817 Persons Bldg., Macon, Ga. Meetings, spring and fall.

Harris, John Warton, Obstetrical Society. (1953) President, E. Russell Muntz. Secretary, Alice D. Watts, 324 E. Wisconsin Ave., Milwaukee 2, Wis.

Honolulu Obstetrical and Gynecological Society. (1947) President, Lyle Bachman. Secretary,

Fugate Carty, Straub Clinic, Thomas Square, Honolulu, Hawaii. Meetings, third Monday of each month at the Mabel Smythe Memorial Bldg.

Houston Gynecological and Obstetrical Society. Secretary, Melville L. Cody, 4115 Fannin,

Houston, Texas.

Indianapolis Obstetrical and Gynecological Society. (1947) President, Carl P. Huber.

Secretary, John F. Spahr, Jr., Suite 902, 23 East Ohio St., Indianapolis 4. Meetings, second Wednesday in January, April, and October (1949) President Polyary C. McDowell.

second Wednesday in January, April, and October.

Interurban Obstetrical and Gynecological Society. (1949) President, Robert C. McDowell, Buffalo, N. Y. Secretary, E. R. Duggan, 16 N. Goodman St., Rochester 7, N. Y. Meeting, Hotel Statler, Buffalo, N. Y., Sept. 22, 1956.

Iowa Obstetrical and Gynecological Society. President, Robert M. Collins, Council Bluffs, Iowa. Secretary, W. B. Goddard, Iowa City, Iowa. Meetings, spring and fall.

Kansas City Gynecological Society. (1922) President, Gerald L. Miller. Secretary, Floyd C. Atwell, 411 Nichols Rd., Kansas City 12, Mo. Meetings, third Thursday, September, November January and March, and first Thursday in May.

November, January, and March, and first Thursday in May.

Kentucky Obstetrical and Gynecological Society. (1947) President, Robert Orr, Mayfield, Ky. Secretary, Ed. Masters, 107 Fairmeade Rd., Louisville, Ky. Annual meeting, spring, 1957.

Long Beach Obstetrical and Gynecological Society. (1954) President, Geneva Beatty.

Secretary, Sydney G. Willner, 911 East San Antonio Drive, Long Beach 7, Calif. Meetings, first Tuesday of March, June, September, and December.

Los Angeles Obstetrical and Gynecological Society. (1914) President, Samuel Martins.

Secretary, Walter C. Rogers, 39 Congress St., Pasadena 2, Calif. Meetings, second Tuesday, September, November, January, March, and May.

Louisville Obstetrical and Gynecological Society. President, J. O. II. Simrall. Secretary, Hugh P. Adking 200 Hayburn Bldg, Louisville 2 Ky. Meetings fourth Monday September, September, March, and May.

Hugh P. Adkins, 920 Heyburn Bldg., Louisville 2, Ky. Meetings, fourth Monday, September, October, November, January, February, March, April, and May.

Madison Obstetrical and Gynecological Society. (1950) President and Secretary, Leonard J. MacKenzie, Gay Bldg., Madison, Wis. Meetings, first Tuesday each month except

July and August.

Maryland, Obstetrical and Gynecological Society of. (1929) President, John Herman Long. Secretary, Harry M. Beck, 700 N. Charles St., Baltimore 1, Md. Meetings, second Thurs-

day, October, December, February, and May.

Memphis Obstetrical and Gynecological Society. (1950) President, John J. Redmon. Secretary, William F. Mackey, 1374 Madison Ave., Memphis, Tenn. Meetings, second Tuesday, October, November, January, March, and May.

- Miami Obstetrical and Gynecological Society. (1946) President, Reuben B. Chrisman.
- Secretary, George R. Gage, 365 Alcazar Ave., Coral Gables, Fla. Meetings, second Thursday, January, March, May, and November.

 Michigan Society of Obstetricians and Gynecologists. (1924) President, Carl F. Shelton. Secretary, E. Bruce Foster, 853 Fisher Bldg., Detroit 2, Mich. Meetings first Tuesday, October to May.
- Milwaukee Gynecological Society. (1951) President, William F. Hovis. Secretary, 1.. T. Servis, 425 East Wisconsin Ave., Milwaukee 2, Wis. Meetings, last Monday, January, March, May, and November.
- Minneapolis Obstetrical and Gynecological Society. (1955) President, John A. Haugen. Secretary, Francis M. Swain.
- Minnesota Obstetrical and Gynecological Society. President, Rodney Sturley. Secretary, Edward A. Banner, 200 First St., Southwest, Rochester, Minn. Meetings, spring and fall. Next meeting, Rochester, Minn., Sept. 22, 1956.

 Mississippi Obstetrical and Gynecological Society. (1947) President, James L. Royals,
- Jackson, Miss. Secretary, J. A. K. Birchett, Jr., P.O. Box 367, Vicksburg, Miss. Meetings May and November.
- Mobile County Obstetrical and Gynecological Society. (1949) President, H. B. Dowling. Secretary, J. R. Mighell, 1302 Government St., Mobile, Ala. Meetings, quarterly when called.
- Montgomery County (Ohio) Obstetrical and Gynecological Society. (1937) President, L. O. Fredericks. Secretary, A. A. Kunnen, 406 Harries Bldg., Dayton, Ohio. third Wednesday of each month.
- Montana Obstetrical and Gynecological Society. (1946) President, Leonard W. Brewer.

 Secretary, Frank Pickett, Box 107, Bozeman, Mont. Annual meeting in spring.

 Nashville Obstetrical and Gynecological Society. (1955) President, Scott Bayer. Secretary,
 H. M. Pace, Jr., 606 Gallatin Rd., Nashville, Tenn. Four meetings per year from October to May.
- Hassau Obstetrical Society. (1944) President, Gerald T. Lilly. Secretary, Andrew S. Sherwin, 64 Hilton Rd., Hempstead, N. Y. Meetings, second Monday, October, December, February, and April.
- New England Obstetrical and Gynecological Society. (1929) President, Carmi R. Alden Secretary, William A. Lynch, 1101 Beacon St., Brookline 46, Mass. Meetings, spring and fall.
- New Haven Obstetrical and Gynecological Society. (1946) President, Robert M. Lewis. Secretary, Fred Gibson, 37 Trumbull St., New Haven, Conn. Meetings, third Tuesday, September, November. January, March. and May.
- New Jersey Obstetrical and Gynecological Society. (1947) President, Sam. Gordon Berkow. Secretary, Paul Grossbard, 162 Lexington Ave., Passaic, N. J. Meetings, October and
- New Mexico Obstetrical and Gynecological Society. (1947) President, M. D. Bivens. Secretary, J. W. Wiggins, 24 Medical Arts Square, Albuquerque. Meetings, quarterly.
- New Orleans Gynecological and Obstetrical Society. (1924) President, Abe Golden. Secretary, C. Gordon Johnson, 3636 St. Charles Ave., New Orleans, La. Meetings, October,
- November, January, March, and May.

 New York Obstetrical Society. (1863) President, Morris A. Goldberger. Secretary, George L. Bowen, 101 East 74th St., New York 21, N. Y. Meetings, second Tuesday, October through May.
- North Carolina Obstetrical and Gynecological Society. (1932) President, R. A Secretary, James A. Crowell, Charlotte, N. C. Meeting last week end in April.
- North Dakota Society of Obstetrics and Gynecology. (1938) President, R. W. Rodgers. Secretary, John Gillam, Box 1388, Fargo, N. D. Next meeting, Oct. 18, 1956.
- Northeastern New York Obstetrical and Gynecological Society. (1935) President, Arthur D. Hengerer, Albany, N. Y. Secretary, Raymond L. Rhodes, 15 W. Notre Dame St., Glens Falls, N. Y. Meetings, February, May, and October.
- Oklahoma City Obstetrical and Gynecological Society. (1940) President, Robert D. McKee. Secretary, James B. Pitts, Jr., 313 Pasteur Medical Bldg., Oklahoma City, Okla. Meetings, third Wednesday of February, April, May, October, and December.

 Omaha Obstetrical and Gynecological Society. (1947) President, Leon S. McGoogan. Secretary, W. H. Taylor, Jr., 3807 Cuming, Omaha, Neb. Meetings, third Wednesday, January, March, May, September, and November.
- Oregon Society of Obstetricians and Gynecologists. President, Gordon McGowan. Secretary, David W. James, 4212 N. E. Broadway, Portland 13, Ore. Meetings, third Friday, October through May, except December.
- Pacific Coast Obstetrical and Gynecological Society. (1931) President, Donald G. Tollefson, Los Angeles, Calif. Secretary, Donald W. DeCarle, 2000 Van Ness Ave., San Francisco, Calif. Next meeting, Oct. 31-Nov. 3, 1956.

Ju

- Pacific Northwest Obstetrical and Gynecological Association. (1947) President, J. E. Harrison. Secretary, Earl L. Hall, 1220 Central Ave., Great Falls, Mont.
 Philadelphia, Obstetrical Society of. (1868) President, George A. Hahn. Secretary, Paul A. Bowers, 2031 Locust St., Philadelphia 3, Pa. Meetings, first Thursday, October through Many 1967. through May.
- through May.

 Pittsburgh Obstetrical and Gynecological Society. (1934) President, William E. Gibson.

 Secretary, John C. Hughes, Schenley Park Apts., Pittsburgh 13, Pa. Meetings, first
 Monday, October through May, except January.

 Portland Society of Obstetricians and Gynecologists. (1928) President, Ivan I. Langley.

 Secretary, James M. Whitely, 1020 S. W. Taylor St., Portland, Ore. Meetings, fourth
 Wednesday, September through May.

 Queens Gynecological Society. (1948) President, J. Gibson Hill. Secretary, David Connors,
 166-05 Highland Ave., Jamaica, L. I., N. Y. Meetings, second Wednesday, October,
 December, February, and April.
- December, February, and April.

 Rochester Obstetrical and Gynecological Society. (1939) President, Donald Kariher. Secretary, Robert A. Clark, 16 N. Goodman St., Rochester, N. Y. Meetings, February, April, September, and December.
- St. Louis Gynecological Society. (1924) President, William H. Vogt, Jr. Secretary, Eugene G. Hamilton, 8505 Delmar Blvd., St. Louis 24. Meetings, second Thursday, October, De-
- cember, February, and April.

 San Antonio Obstetrical and Gynecological Society. President, G. G. Passmore. Secretary, Frank M. Posey, Jr., 641 Moore Bldg., San Antonio. Meetings, first Monday of the month.

- San Diego Gynecological Society. (1937) President, George H. Derieux. Secretary, Wilton Lewis, 525 Hawthorn, San Diego 1, Calif. Meetings, as announced.

 San Francisco Gynecological Society. (1929) President, Charles T. Hayden. Secretary, Edmund F. Anderson, 2445 Ocean Ave., San Francisco 27, Calif. Meetings, second Friday, October through April.

 Seattle Gynecological Society. (1941) President, Albert Lee. Secretary, John Clancy, 1010 Boylston, Seattle 4, Wash. Meetings, third Wednesday of each month, except summer months. months.

- Months.
 South Carolina Obstetrical and Gynecological Society. (1946) President, Herbert Blake. Secretary, James E. Bell, 325 W. Calhoun St., Sumter, S. C. Meeting, spring.
 Southwest Obstetrical and Gynecological Society. (1951) President, Hollis Brainard, Tucson, Ariz. Secretary, Zeph B. Campbell, 550 W. Thomas Rd., Phoenix, Ariz. Annual meeting, Tucson, Ariz., Nov. 12 and 13, 1956.
 Texas Association of Obstetricians and Gynecologists. (1930) President, Carey Hiett, Fort Worth, Texas. Secretary, Oran V. Prejean, 4317 Oak Lawn Ave., Dallas 19, Texas. Annual meeting, February, 1957.
 Tulsa Obstetrical and Gynecological Society. (1955) President Divon Burns. Secretary
- Tulsa Obstetrical and Gynecological Society. (1955) President, Dixon Burns. Secretary, J. E. Goldberg, 1980 Utica Square, Tulsa, Okla. Five meetings per year. Utah Obstetrical and Gynecological Society. (1948) President, Morgan S. Coombs. Secretary, Von G. Holbrook, 508 East South Temple, Salt Lake City 2. Meetings, second Tues-
- day of October, December, March, and May, or as announced.

 Virginia Obstetrical and Gynecological Society. (1936) President, George S. Hurt. Secretary, Chester D. Bradley, 2914 West Ave., Newport News, Va. Meetings, April and October.
- October.

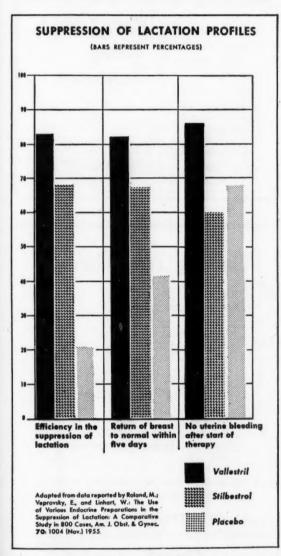
 Washington Gynecological Society. (1933) President, J. Keith Cromer. Secretary, Robert B. Nelson, Jr., 1824 Massachusetts Ave., N. W., Washington, D. C. Meetings, fourth Saturday in October, November, January, March, and May.

 Washington State Obstetrical Association. (1936) President, Robert M. Campbell. Secretary, Glen G. Rice, 803 Medical Dental Bldg., Seattle 1, Wash. Meetings, Oct. 20, 1956, Yakima, Wash., and April 13, 1957, Vancouver, B. C.

 West Texas Obstetrical and Gynecological Society. (1954) President, O. R. Hand, Lubbock, Texas. Secretary, D. D. Wall, 234 W. Beauregard Ave., San Angelo, Texas. Meeting, Dec. 6, 1956, Lubbock, Texas.

- Wisconsin Society of Obstetrics and Gynecology. (1940) President, Dean D. Willson, Fond du Lac, Wis. Secretary, William V. Luetke, 1023 Regent St., Madison 5, Wis. Meetings, spring and fall.

A New 20-mg. VALLESTRIL® Tablet for the suppression of lactation



Comparison of control patients with those receiving Vallestril indicates its merit.

The success of Vallestril in suppressing lactation has indicated the desirability of a new and more convenient dosage form. Searle's new 20-mg. tablet meets this requirement. Only two of the 20-mg. tablets taken daily, for five days, suppress lactation and relieve engorgement and pain.

Shook* states: "Vallestril does prevent breast symptoms and lactation initially, is not followed by secondary lactation and breast engorgement, does not result in withdrawal bleeding and does not inhibit normal involution of the uterus."

Vallestril (brand of methallenestril) is a single chemical substance of high estrogenic activity, but with relative freedom from the side effects of nausea, withdrawal bleeding, edema and other adverse reactions associated with other estrogens. These advantages of Vallestril make it preferentially useful, not only in suppression of lactation, but in other conditions in which estrogen therapy is indicated.

Vallestril is now supplied in two forms: 20mg. tablets and 3-mg. tablets. Dosage for indications other than the suppression of lactation is supplied in Reference Manual No. 7. G. D. Searle & Co., Research in the Service of Medicine.

*Shook, D. M.: Management of Suppression of Lactation, to be published.

Clinical trial sample of Vallestril 20-mg. tablets and literature available on request to . . .

SEARLE

P. O. Box 5110-E1 Chicago 80, Illinois

This is the ORIGINAL

contraceptive

creme

with a record of

22 years

of successful use!



We are prepared to consider requests from professionally qualified investigators for experimental quantities of vitamin E in the form of d-alpha-tocopherol or its derivatives. Address inquiries to: Dr. Norris D. Embree, Director of Research, Distillation Products Industries, Rochester 3, N. Y. (Division of Eastman Kodak Company).



supplier of bulk tocopherols to the pharmaceutical industry

Booklet for patients

Your Care during Pregnancy

Practicing physicians are invited to ask for sample copy without obligation. Medically sponsored text. Used for a decade by thousands of leading doctors throughout United States and Canada. Write—

CADUCEUS PRESS

222 Nickels Arcade, Ann Arbor, Mich.

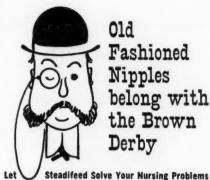
Changing Your Address?

When you move, please-

- (1) Notify us to change your address allow us six weeks to make the change.
- (2) Mention the name of this Journal. (We publish twelve periodicals.)
- (3) Give us your old address. If possible, return the addressed portion of the envelope in which we sent your last copy.
- (4) Give us your new address—complete —including the Postal zone number.
- (5) Please print your name and address.

Thank You!

Circulation Department, The C. V. Mosby Company, Publishers, 3207 Washington Blvd., St. Louis 3, Mo.



Old Fashioned Nipples belong with the Brown Derby

Professionally Used and Recommended

STEADIFEED NIPPLES

They Need No adjustment They Can't Leak They Won't Pull Off

Helps Prevent Nursing Colic, Gas, Excessive Burping

Write for FREE Professional Sample



THE NIPPLE THAT B.R.E.A.T.H.E.S SEARER RUBBER CO., Akron 4, Ohio NURSERS 25c

The GREENBERG FOAM RUBBER MITTEN*

An American Contribution toward Safer Obstetrics



*As described in June 1953 issue of Surgery, Gynecology and Obstet-rics, Greenberg, Eman-uel, M.D.: Surg., Gynec. Obst., 1953, 96: 754.

helps eliminate obstetrical forceps marks on newborn babies.

Simple to Use Easy to Apply Can be Sterilized Foam Rubber Construction

> AT YOUR SURGICAL DEALER

Distributors

BITTNER CORPORATION 109 Worth St., New York 13, N. Y.

> **GRAHAM-FIELD** 32-56 62nd St., Woodside 77, N. Y.

One out of three who died of cancer last year could have been saved?

> To alert the practicing physician to suspect and diagnose cancer early the American Cancer Society has available for you a film series of Physicians' Conferences on Cancer.

*Kinescopes of live, color, closed-circuit television programs, on early diagnosis and treatment of cancer, present outstanding clinicians.

These 24 film programs - the nucleus of a course on cancer for the General Practitioner - cover virtually all cancer sites and types. They center around panel discussions, laboratory techniques, case histories, x-ray findings, histopathology, statistical data, and operative procedures.

Professional Films and services available to the doctor in his own community may be obtained through your Division of the

American Cancer Society

* APPROVED BY THE AMERICAN ACADEMY OF GENERAL PRACTICE FOR INFORMAL STUDY CREDIT (16 MM COLOR SOUND FILMS, RUNNING TIME 30-50 MINUTES)



It's actually easy to save—when you buy Series E Savings Bonds through the Payroll Savings Plan. Once you've signed up at your pay office, your saving is done for you. The Bonds you receive pay good interest—3% a year compounded half-yearly when held to maturity. And the longer you hold them, the better your return. Even after maturity, they go on earning 10 years more. So hold on to your Bonds! Join Payroll Savings today—or buy Bonds where you bank.

Safe as America – U.S. Savings Bonds



DIAGNOSIS:

knife wound in the heart



Under the blazing blue sledge hammer of a Chicago heat wave, the cramped, makeshift operating room shimmered like an oven, reeking of ether and carbolic. Six sweat-drenched, frock-coated doctors huddled in fascination, watching deft hands reach into a human chest and expertly stitch up a fluttering wound in the redness of a pulsing heart.

Would he live? The surgeon mopped his brow and hoped. The year was 1893; the operation, fantastic.

Live? Yes, he would live for many more years, thanks to the skill and courage of Dr. Daniel Hale Williams.

Abandoned as a child, Williams, a Negro, had struggled hard for an education. Now only 37, he had already founded America's first interracial hospital, Provident. And here he had just performed the first of the pioneering operations that would mark him as one of our country's great surgeons.

Sensitive and brave, Daniel Hale Williams was blessed with an abundance of the same urge to help his fellow man that binds and strengthens Americans today.

And it is these strong, unified Americans who are our country's real wealth—the real backing behind our nation's Savings Bonds. In fact, they're the true reason why U. S. Savings Bonds are considered one of the world's finest, safest investments.

For your own security—and for America's —why not invest in Savings Bonds regularly? And hold on to them!

The U.S. Government does not pay for this advertisement. It is donated by this publication in cooperation with the
Advertising Council and the Magazine Publishers of America.

Nu-lift's* shoulder straps

GIVE NATURAL
"HAMMOCK" SUPPORT,
GREATER COMFORT

Baby's head low in pelvis. Bladder pressure, stretching of abdomen, acute angle of the back.

RIGHT: Nu-Lift supported Pregnancy: Baby is elevated, body is erect, intra-pelvic pressure lessened. Bulging, stretching minimized, backache relieved, possibility of varicosities lessened.

* PATENT #2,345,760



MATERNITY
SUPPORTS
and brassieres

LITERATURE AND SAMPLE AVAILABLE UPON REQUEST

NU-LIFT COMPANY, INC.

Dept. J-7, 1021 N. Las Palmas, Hollywood 38, Calif.



LIGHTWEIGHT NO HEAVY BONING



CRISS-CROSS INNER BELT minimizes backache, improves posture, gives support and comfort in sacroiliac and lumbar regions.



SEPARATE POST-PARTUM PANEL aids organs and muscles in their return to normal. Included with garment.

\$12.50 COMPLETE at leading department and maternity stores.



END THE TORTURE

of agonizing vulvar itch in monilial vaginitis!

FAST, WELCOME RELIEF HIGH RATE OF CURE

Vaginal Anti-infective Jelly. Contains 0.1% gentian violet in an acid polyethylene glycol base.

Once nightly — just 12 applications usually cures the most stubborn case

GA-4

WESTWOOD PHARMACEUTICALS . Div. Foster-Milburn Co. . 468 Dewitt St., Buffalo 13, N. Y.

for normal, healthy, comfortable pregnancies



PHOSPHORUS-FREE, HIGH-POTENCY DRY-FILL* CAPSULES WITH "BUILT-IN" ANTIANEMIA FACTORS *Micropulverized dry powder fill, for better toleration, faster assimilation and absence of fishy after-taste.

Walker LABORATORIES, INC., MOUNT VERNON, N.Y., U.S.A.

INDEX TO ADVERTISERS

Please mention "The American Journal of Obstetrics and Gynecology" when writing to advertisers—it identifies you

Abbott Laboratories 16,	27	Lilly and Company, Eli	54
American Cancer Society	57	Lloyd Brothers, Inc 38,	39
American Sterilizer	45	Marie Control of the Control of the Control	
Arnar-Stone Laboratories, Inc.	3	Massengill Company, The S. E.	15
Ayerst Laboratories 10.	36	Insert between pages 48 and	49
		Massengill Company, The S. E 11,	33
Bard-Parker Company, Inc.	2	Mead Johnson & Company	1
Borden Company, The Fourth Co			
Boyle & Company	42	National Drug Company, The	
	4	Insert between pages 32 and	33
Burroughs Wellcome & Company (U. S. A.), Inc.	14	Nu-Lift Company, Inc.	59
Caduceus Press	EC	Organon, Inc.	7
Carnation Instant Milk	26		
Ciba Pharmaceutical Products, Inc.	20	Parke, Davis & Company	35
Second Co	ver	Pet Milk Company	22
Ciba Pharmaceutical Products, Inc.	47	The same of the same of the same	
		Riker Laboratories	20
Davis & Geck, Inc.	41	Roussel Corporation	53
Desitin Chemical Company	40		
Distillation Products Industries	56	Schering Corporation 28,	29
Doho Chemical Corporation	5	Schmid, Inc., Julius	44
		Searer Rubber Company	57
Eaton Laboratories 15,		Searle & Company, G. D.	
Esta Medical Laboratories, Inc.		Sharp & Dohme	
Ethicon, Inc Insert between pages 4 and	d 5	Smith, Kline & French Laboratories 25,	
Garat Chambal Garage	40	Smith, Kille & Flench Laboratories 25,	02
Grant Chemical Company	43	United States Savings Bonds	58
Greenberg, Dr. Emanuel	57	Cinted States Savings Donds	90
Hoffmann-La Roche, Inc.		Walker Laboratories, Inc.	60
Insert between pages 16 and	17	Warner-Chilcott Laboratories9.	
Hoffmann-La Roche, Inc.	24		
Holland-Rantos Company, Inc.	32	Webster Company, The William A	
		Westwood Pharmaceuticals	59
Kidde Manufacturing Company	34	White Laboratories, Inc. 23, 50,	
Kinney & Company, Inc.	31	Whittaker Laboratories, Inc.	10000
		Whittier Laboratories 18,	
Lederle Laboratories	17	Winthrop Laboratories	37

While every precaution is taken to insure accuracy, we cannot guarantee against the possibility of an occasional change or omission in the preparation of this index.

for normal, healthy, comfortable pregnancies



PHOSPHORUS-FREE, HIGH-POTENCY DRY-FILL* CAPSULES WITH "BUILT-IN" ANTIANEMIA FACTORS *Micropulverized dry powder fill, for better toleration, faster assimilation and absence of fishy after-taste.

Walker LABORATORIES, INC., MOUNT VERNON, N. Y., U. S. A.

INDEX TO ADVERTISERS

Please mention "The American Journal of Obstetrics and Gynecology" when writing to advertisers—it identifies you

Abbott Laboratories 16,	27	Lilly and Company, Eli	54
American Cancer Society	57	Lloyd Brothers, Inc 38,	39
American Sterilizer	45		
Arnar-Stone Laboratories, Inc	3	Massengill Company, The S. E	
Ayerst Laboratories 10,	36	Insert between pages 48 and	49
		Massengill Company, The S. E 11,	33
Bard-Parker Company, Inc	2	Mead Johnson & Company	1
Borden Company, The Fourth Cov	er		
Boyle & Company	42	National Drug Company, The	
Bronstein, Harry	4	Insert between pages 32 and	33
Burroughs Wellcome & Company (U. S. A.), Inc.	14	Nu-Lift Company, Inc.	59
Caduceus Press	56	Organon, Inc.	7
Carnation Instant Milk	26	Parke, Davis & Company	35
Ciba Pharmaceutical Products, Inc.		Pet Milk Company	22
Ciba Pharmaceutical Products, Inc.		ret Mik Company	
Ciba Fharmaceutical Froducts, Inc	47	Riker Laboratories	20
Davis & Geck, Inc.	41		53
	40	Roussel Corporation	93
	56	2.1.1. G	0.0
Doho Chemical Corporation	5	Schering Corporation 28,	
Dono Chemical Corporation Linearing	0	Schmid, Inc., Julius	
Eaton Laboratories 15,	49	Searer Rubber Company	
	21	Searle & Company, G. D.	55
Ethicon, Inc Insert between pages 4 and	5	Sharp & Dohme	13
		Smith, Kline & French Laboratories 25,	52
Grant Chemical Company	43		
Greenberg, Dr. Emanuel	57	United States Savings Bonds	58
Hoffmann-La Roche, Inc.		Walker Laboratories, Inc.	60
Insert between pages 16 and	17	Warner-Chilcott Laboratories 9,	
Hoffmann-La Roche, Inc.	24		12
Holland-Rantos Company, Inc	32		59
	34	White Laboratories, Inc. 23, 50,	
Kinney & Company, Inc.	31	Whittaker Laboratories, Inc.	-
		Whittier Laboratories 18,	
Lederle Laboratories	17	Winthrop Laboratories	37

While every precaution is taken to insure accuracy, we cannot guarantee against the possibility of an occasional change or omission in the preparation of this index,

JEANES HOSPITAL

either way you win with Bremi

"heads"...because a BREMIL formula provides a complete nutritional intake that consistently promotes infant growth and development at or above accepted standards¹; made with grade A milk.

"tails"... because the easily digested, efficiently utilized protein content of BREMIL (approximating that of breast milk) virtually eliminates exceptations due to ammonia

dermatitis¹, and does not impose an excessive solute load on the immature kidney²

Standard Dilution

One level measure to 2 fluidounces of hot water. Mixes like a liquid. Costs no more than ordinary formulas requiring vitamin and carbohydrate supplementation. In 1-lb. tins at all drug outlets.

Borden's

PRESCRIPTION PRODUCTS DIVISION 350 Madison Avenue, New York 17



 Oberman, J. W., and Burke, F. G.: M. Ann. District of Columbia 23:483, 1954.
 Hill, L. F.: Am, J. Clin. Nutrition 3:75, 1955.

